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• T. Rowland Hill, 'The Medical Press' 5981, 628, December 1953.

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CONSTIPATION*

R. SCHAFFER, M.A., M.D.

Queenstown

The Trades Exhibition is an essential part of a successful Medical Congress and the members of the Medical Association have reason to be grateful to our friends the Trade Exhibitors who make our Congresses so interesting and instructive. This morning one of the exhibitors handed me a beautifully illustrated and well printed brochure entitled 'Constipation—Its Types and Therapy'. This little book contains some very useful information about a subject which has been very much neglected by our teachers of medicine. The coloured illustrations suggest that *Homo sapiens* may have a very attractive interior, particularly if regular use is made of a very elegant and well advertized American preparation which is the treatment of choice in all cases.

Homo sapiens is indeed a queer creature, distinguished from other mammals not only by its peculiar posture. There are other characteristics. The human animal differs from most other creatures in that it, and it alone, is interested in its excreta. The newborn baby may be microcephalic or hydrocephalic, but this may not be noticed by the mother, who seems more concerned over the infant's stools. The colour, the frequency and even the odour of the newborn's excreta are, I am informed, some of the less noxious subjects discussed at fashionable mothers' tea parties. The infant shares its mother's pride when the stool is yellow and well formed and shares parental anxiety when symptoms resulting from paternal rejection or maternal engulfment are attributed to constipation. The child is thus, from its earliest days, conditioned to become a bowel-conscious adult.

It becomes part of its credo that bowels should act every day, but there is so much else to do that the urge to defaecate is suppressed; it also happens that urge and opportunity do not always coincide. Houses and families may be large, but lavatories few, and frequently occupied. School lavatories are also not very inviting and not free when required. The child, which is conscious of its negligence, resents the circum-

* A paper presented at the South African Medical Congress, Pretoria, October 1955.

stances which make its bowel negligence inevitable. Even in the infant frustration and resentment are the main causes of psychosomatic disturbances, and the gastro-intestinal system is most frequently disturbed. Bowel motility is altered, and the bowel-conscious child grows into the colospastic or dyschezic adult.

Constipation can be defined as the condition in which there is delay in the evacuation of faeces, resulting in the passage of hard, dry stools. This may be due to or associated with gross organic disease, which must in every case be excluded. In the majority of cases no organic cause can be detected.

It is essential to know that the pattern of bowel evacuation varies with the individual. Once a day is normal for most, twice a day for others and twice a week for some.

The superstition that bowel contents are toxic and that health is promoted by keeping the bowel empty is nonsense. Excessive purgation interferes with bowel function and with health. The right half of the colon should always contain food residue. Cellulose is partially digested by bacterial activity and rendered non-irritating, and excess fluid is absorbed. Excessive motility of caecum and colon is responsible for excessive gas formation. A colon without residue is a colon full of gas. The normal function of the distal colon is storage and expulsion and there should be no interference with normal function.

Dyschezia

Normal defaecation is a conditioned reflex and failure to develop and maintain regular habits may lead to a breakdown of the reflex mechanism, as a result of which rectum and pelvic colon can become tightly packed and distended with a hard faecal mass. This condition is known as dyschezia and is very much commoner than is generally believed. Purgatives do not dislodge this mass, but will force a canal through the mass of faeces through which liquid bowel-contents can escape. The symptoms are abdominal pain and discomfort, headache, backache, lassitude and nausea; these are not caused by toxæmia as used to be believed,

and can also be produced by packing the rectum with cotton wool. It is not unusual to find a rapidly emptying stomach and a spastic colon associated with an over-distended pelvic colon and rectum. Unfortunately the diagnosis is often missed because the patient is not properly examined. Rectal examination is essential both in young and old. It cannot be repeated too often that 'if you do not put your finger into it, you put your foot into it'. The following case illustrates a very advanced form of this condition, but a clinical history of this type is not unusual.

Mrs. X, aged 38, was referred to me by a colleague, who had diagnosed an ovarian cyst. The patient was very anxious to have surgical treatment. She was an obese married woman with 2 children, aged 6 and 8. The confinements had been normal and there was nothing abnormal in the menstrual history. She had been constipated since her schooldays and always complained of cramp-like abdominal pains. She had been swallowing laxative pills, liquid extract of cascara and, on special occasions, castor oil, for as long as she could remember.

The appendix had been removed when she was 18 years old, and the gall-bladder when she was 28. She informed me with great pride that it had been a most abnormal gall-bladder and that the surgeon had had great difficulty in disentangling adherent stomach, bowel and liver. Two years later she had an operation for adhesions. (It should be more generally known that adhesions which do not cause obstruction usually cause no symptoms. Those who suffer from excessive surgical libido should remember that what the Lord has joined together, no man shall put asunder.) The year after her first confinement a ventral suspension was done and a cyst removed from the right ovary. (It is only very seldom that a ventral suspension is indicated and it seems most unlikely that this was such a case.)

She now complained of severe backache, dysuria, dysparunia and pain in the region of the left iliac fossa.

Examination revealed a much-scarred abdomen, normal chest and cardio-vascular system, and normal urine. A mass the size of a small melon could be felt in the left iliac fossa and could be moved from side to side. On vaginal examination this mass had the characteristics of an ovarian cyst. The rectum was tightly packed with faeces, but I did not consider this of major importance at the time.

On opening the abdomen I found an enormously distended pelvic colon. The abdomen was closed, the patient put into lithotomy position and a flushing curette introduced into the rectum. It took almost an hour of flushing and digital manipulation of the faecal mass to clear the bowel. A sanitation specialist might perhaps have done the work more expeditiously.

The patient was extremely satisfied with the result and I was given great credit for my diagnostic skill and surgical ability.

Laparotomy, of course, is not as a rule the treatment of choice and I have not again found it a necessary diagnostic procedure, but I have frequently done the operation of digital removal of faeces under general anaesthesia. The mass should first be softened and lubricated with an enema of warm oil. Once the bowel is emptied it is essential to re-educate the bowel, which can be a slow and difficult process. Giving enemas of glycerine and water, which must gradually be reduced in strength, quantity and frequency is very useful. Purgatives must be avoided.

Spastic Constipation

Spastic constipation results from emotional disturbances, is aggravated by menopausal or other endocrine dysfunction, and is made worse by purgatives, enemas and excessive exercise. An enema cannot remove frustration and a purgative is no cure for marital maladjustment. A diet containing too much roughage is

also harmful. Successful treatment requires low-residue diet with sufficient protein and vitamins, an adequate fluid intake, explanation and reassurance. Sedatives and antispasmodics are helpful, but should play a minor part in treatment. The following case illustrates the condition.

An unmarried teacher aged 40 (female) gave the following history: She had suffered from abdominal discomfort and occasional severe colicky abdominal pain for the past 15 years. She did not marry, because she was the youngest daughter of a large family and had to stay at home and look after her invalid mother (now deceased). She had always been constipated and always suffered from 'indigestion'. She felt very unhappy unless she swallowed milk of magnesia, the action of which was occasionally augmented with cascara or Beecham's pills. Her appendix had been removed 10 years previously and a ventral suspension had been done at the same time. Haemorrhoids had been injected 2 years later but they were still troublesome. Menstruation had lately become more frequent and there was very considerable dysmenorrhoea. She was referred to me by a colleague, who suggested I should investigate her condition with a view to advising another surgical procedure.

Examination revealed an undernourished, anxious-looking, obviously frustrated female. Her teeth had long been replaced by ill-fitting dentures. There was a slight tremor of the tongue. She had tachycardia but there was no evidence of hyperthyroidism or organic cardiac disease. There was tenderness on palpating the caecum and sigmoid colon. Rectal examination showed no significant abnormality and urine was normal. X-ray examination revealed a rapidly-emptying posited stomach, a rapidly-emptying small intestine, and a very spastic caecum and colon. Barium enema showed a few small diverticulae, but no other abnormality.

This lady was given a low-residue, high-protein diet, a vitamin supplement and pill Bellergal (belladonna, phenobarb and ergotamine) *t.d.s.* Her condition has improved very considerably, though she still enjoys bad health.

Treatment

The drug addict and the chronic alcoholic are difficult to treat; it is even more difficult to treat the pill-and-purgative addict. These cases frequently require hospitalization and prolonged supervision.

In the old and debilitated, constipation is usually associated with an atonic bowel. Re-education is no longer possible. The 'enjoyment of bad health' may be the only pleasure left to the patient, and the bowel habits of a lifetime should not be lightly disturbed. When pills and purgatives have been used for many decades they have done all the harm they can do and no useful purpose will be served by depriving the old of something which they consider essential. When dealing with the old, the doctor must not attempt to change the habits of a lifetime; he will not change the patient, but the patient may change the doctor. It is, however, necessary to stop a liquid-paraffin habit. This apparently innocuous and chemically inert oil prevents absorption of vitamins and interferes with the absorption of nourishment. The habitual use of this mineral oil can be harmful both in old and young. Constipation, and the symptoms attributed to constipation, in the old are often relieved by treating a minor degree of hypothyroidism, and by correctly treating a previously unsuspected congestive cardiac failure.

The young must be taught the importance of regular habits, and must learn that punctuality is important in all things. The adult must use laxatives only occasionally. The innocent well-advertized pill may be habit forming.

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VAN DIE REDAKSIE

MOORD EN DIE DOODSTRAF

Is 'n moordenaar die dood skuldig vir sy misdaad? Hierdie eeu-oue vraag het die aandag gevestig van akademici, teoloë en leke in elke geslag en weereens vlam belangstelling daarin op in Wes-Europa, veral in Brittanje, waar 'n debat oor 'n mosie om die doodstraf af te skaf binnekort deur die Parlement gevoer sal word. Baie lande van Europa, asook Portugal met inbegrip van haar gebiede in Afrika, het die doodstraf afgeskaf. In enige moordsaak is die mediese getuienis van lewensbelang—dikwels hang die beskuldigde se lewe (of sy lot) daarvan af. Mediese kringe in Suid-Afrika behoort in hierdie huidige veldtog in Brittanje belang te stel.

Die vraagstuk kan vanuit verskeie oogpunte benader word. In beginsel kan aangevoer word dat 'n beskaafde gemeenskap vergelding vir 'n antisosiale daad—veral vir so 'n afskuwelike een—moet en sal eis. Dit kan beskou word as primitief en nie in volle ooreenstemming met Christelike beginsels nie om vir redes van wraak of vergelding straf toe te pas of om die misdadiger net so te laat ly soos hy sy slagoffer laat ly het. Desnieteenstaande is dit 'n grondgedagte dat die straf deur die misdaad bepaal moet word. (Die geldigheid van hierdie begrip word nie betwis nie wanneer versagende omstandighede aangevoer word om 'n ligter vonnis te verkry). Dit is 'n grondbeginsel van vergelding dat die gemeenskap op plegtige en dramatiese wyse sy afsku aan moord moet betuig deur moordenaars swaar te straf; dit bedoel nie dat die gemeenskap noodwendig moordenaars tot die dood moet veroordeel nie.¹

Alvorens die manier van straf bespreek word is dit nodig om die aard van die misdaad te oorweeg. Moord word beskou as wederregterlike, doelbewuste en opsetlike manslag; dit moet bewys word dat ten tye van die misdaad die moordenaar ten volle beseft het wat hy doen. Kan dit altyd onomstootlik bewys word? Die aantal persone wat elke jaar vir moord tereggestel word is miskien die beste aanduiding dat die howe oortuigende bewyse vind. Elke medikus wat al in die getuiebanc moes staan sal egter getuig dat dit moeilik is om of die opset of die gesondheid van verstand te bewys.

Die kwessie van geestesgesondheid vereis gewoonlik deskundige psigiatryse getuienis en die mening van een geneesheer kan hemelsbreed verskil van 'n ander. Bowendien verskaf die geregtelike maatstaf vir krankinnigheid (die eeu-oue McNaughton-reëls, wat dikwels aanleiding gee tot geskille tussen psigiaters en regsgeleerdes) geen tasbaarder hulp aan die regsbank as

EDITORIAL

MURDER AND THE DEATH PENALTY

Should a murderer forfeit his life for his crime? The age-old controversy has exercised the minds of academicians, theologians and laymen alike in every generation, and it has now once more come to the fore in western Europe, and particularly Britain, where Parliament will shortly debate a motion calling for the abolition of capital punishment. In many European countries, including Portugal, with its African territories, the death penalty no longer exists. The medical evidence in any murder trial is always vital—frequently the accused (or his fate) hangs on the doctor's evidence and the renewed campaign in Britain should evoke interest in South African medical circles.

One can discuss the matter at various levels of thought. Fundamentally it can be said that a civilized society must, and will, demand some sort of retribution for an anti-social act, particularly one so heinous as murder. It is considered primitive and sub-Christian to regard retribution or revenge as a motive for punishment, or to make the criminal suffer what he has inflicted on others. Nevertheless there is an underlying idea that punishment should bear some relation to guilt. (No one doubts the validity of this concept when it is used to justify the reduction of a sentence because of mitigating circumstances.) 'The principle of retribution demands that society shall solemnly and dramatically express its abhorrence of murder by imposing a grave punishment on murderers; it does not necessarily mean that society must kill murderers'.¹

Before discussing the form of the punishment, it is necessary to examine the nature of the crime itself. Murder is taken to be the unlawful killing of another human being, and it has to be shown that the murderer fully intended to kill his victim, and that he knew what he was doing at the time. Can this always be proved convincingly? The number of persons hanged each year for murder is perhaps the best indication that it is proved to the satisfaction of the courts, but any medical man whose duties lead him to the witness box will testify to the difficulties involved in proving either sanity or intent.

die opvattinge van psigiaters nie. As regsdwalinge nie voorkom nie moet dit aan die wysheid van ons regters te danke wees; die mening van 'n skerpsinnige leek kom somtyds meer verstandig voor en nader aan die waarheid as die mening van 'n mediese getuie. Om te bewys dat die beskuldige bedoel het om die misdaad te pleeg is suiwer 'n regskwessie en tog is dit net so moeilik om dit te bewys as om te bewys dat die beskuldige by sy volle verstand was en regsredenasie is somtyds eenaardig. 'n Gewapende inbreker wat iemand om die lewe bring word gewoonlik as 'n moordenaar beskou en tog word aanranders in die meeste noodlottige skollie-gevegte in Kaapstad slegs aan manslag skuldig bevind—die bevinding lui in sulke gevalle dat die aanrander nie bedoel het om sy teenstander dood te maak nie. Tradisionele geloofsoortuiging mag 'n lewensbelangrike faktor wees, en tog in die geval van rituele moorde wat dikwels in natuurelgebiede in Afrika voorkom word die faktor oënskynlik oor die hoof gesien, ten minste in sekere lande, alhoewel 'n sterk geloof nie die toorkuns in Suid-Afrika by die houe aanvaar word as rede om die straf te versag. Dit kan geredeneer word dat die primitiewe natuurel nie daarin kon of wou slaag nie om die oppergesag van die blanke se *pax* te aanvaar nie. Oorheers die barbaar se oer-oue drang om die geeste van sy voorvaders tevrede te stel nie alle ander eise nie? Voel hy nie dat dit beter is om sy eie nietige lewe prys te gee nie eerder as om die toorn van sy voorvaders se geeste op homself neer te haal nie? Is 'n aanklag van moord onder sulke omstandighede redelik? Die ondervinding leer dat moord selde 'n onvoorwaardelike diagnose is maar die behandeling wel.

Om nou die straf te bespreek; dat die straf in verhouding tot die misdaad moet staan beteken geensins dat die dood met die dood geboet moet word nie. In Suid-Afrika word moordenaars sedert die vroegste tye tot die dood veroordeel, maar die ingang van moderne opvattinge het in baie lande gelei tot die afskaffing van die doodvonnis as 'n vorm van geregtelike straf. Dit is hoofsaaklik te danke aan die oortuiging—wat gestadiglik posgevat het as gevolg van ondervinding en wat beklemtoon is deur die British Royal Commission van 1953 (wat ondersoek ingestel het in die statistiek van lande wat die doodstraf afgeskaf het)—dat hierdie statistiek nie kan bewys nie of daar 'n verhouding tussen doodstraf en moord bestaan of nie. Met ander woorde, die verstandige opvatting dat die vooruitsig van die doodstraf 'n persoon van moord sal afskrik, word nie deur statistiek bewys nie. Daar vind vandag baie moorde plaas onder omstandighede wanneer verstandige denke onwaarskynlik is bv. persoonlike twistes, drank, seks, e.d.m. en die gewig wat aan die doodstraf as afskrifmiddel toegeskryf word, moet buite rekening gelaat word. Die feit bly egter staan dat dit nog nie finaal bewys is nie dat die gedagte aan die doodstraf miskien nie elke jaar moontlike misdadigers van moord afskrik nie. Britse regters is daarvan oortuig dat werklik geharde professionele misdadigers om dié rede geen vuurwapens dra nie.

As doodstraf nie die misdadiger afskrik nie, wat staaf andersins die bestaan daarvan? Wraak? As die reaksies van die publiek op sensasiewekkende nuusverhale enige

The problem of sanity usually calls for expert psychiatric evidence, and here the opinion of one doctor may be exactly opposite to that of another. Moreover, the legal yardstick of sanity—the century-old McNaghten rules, which often lead to difference of opinion between lawyers and psychiatrists—offers the bench no more concrete material than the views of psychiatrists. If there are no miscarriages of justice the fact must be attributed to the wisdom of our judges. It sometimes seems as if the opinion of a shrewd layman on the 'sanity' of an individual is more sensible and nearer the mark than that of a medical witness.

The proof of intent is a pure legal matter, yet it is little clearer than that of sanity, and the law may indulge in some strange reasoning. An armed man breaking into premises and killing someone is usually regarded as a murderer, yet the assailants in most fatal skolly-brawls in Cape Town are found guilty of culpable homicide only—the intent to kill is held to be missing. The traditional beliefs of the assailant may be a vital factor, yet in another common type of African murder—the ritual murder of the Native territories—it is apparently ignored, at least in some countries, though now in South Africa a strong belief in witchcraft would serve as an extenuating circumstance, reducing the penalty. Here, it can be argued, the primitive essentially African mind of the accused has failed or refused to accept the supremacy of the white man's *pax*. Does not the primeval urgency of satisfying the tribal gods transcend all other considerations to a savage? Does he not feel, philosophically, that it is better to lose his own puny life than to call up the wrath of his ancestors upon himself? And is it a rational act to indict this individual on a charge of murder? On the basis of experience one may conclude by saying that murder is hardly ever an absolute diagnosis; only the treatment is absolute.

Now to consider the punishment: That the punishment should fit the crime does not necessarily imply that death must be met by death. In South Africa the death penalty has been imposed since the earliest times for the crime of murder, but the spread of modern thought has in many countries led to the abolition of the death penalty as a legal form of punishment. The main reason for this has been the conviction—slowly reached by experience and emphasized by the British Royal Commission of 1953 (which examined statistics from countries where penal killings had been abolished)—that statistics afford no evidence one way or another whether there is a connection between the death penalty and the murder rate. In other words, the common-sense opinion that the prospect of having to die for an action may deter a person from doing it is not statistically proved. Today many murders occur in circumstances where such reflections are unlikely; e.g. personal quarrels, drink, sex, etc.; and the value of the death penalty as a deterrent is to be discounted. The fact remains, however, that it is not finally proved that many potential criminals are not each year discouraged from murder by the prospect of hanging; British judges are convinced that really hardened professional criminals are deterred from carrying firearms for this reason.

If the deterrent value of hanging is removed, what else is there to support it? Revenge? If the public's

aanduiding is, dan is die antwoord ja. Wanneer die besonderhede van 'n grusame moord ontbloeit word, hoor mens so dikwels, 'hy behoort net so behandel te word' of, 'ophang is te goed vir hom'; dit is in werklikheid suiwer wraakgedagtes. 'n Belangrike praktiese aspek in enige poging om die doodstraf af te skaf is die openbare mening. Daar moet rekening gehou word met die gevaar dat indien die staat weier om die moordenaar tereg te stel die drang na wraak daartoe aanleiding sal gee dat die publiek die wet in hul eie hande sal neem. In 'n gemeenskap van veelvoudige rasse waar 'n rasse moord vlammende haat kan laat oplaai mag dit wel 'n sterk argument ten gunste van die behou van die doodstraf wees. Afgesien van openbare gevoelens egter moet die kwessie of die doodstraf behou moet word beslis word deur die waarde daarvan as afskrikmiddel.

¹ *Daily Telegraph*, Londen. 10 Januarie 1956.

reaction to sensational news stories is any indication, then the answer is Yes. When the details of an atrocious murder are disclosed, how often does one not hear, 'He ought to be treated in the same way', or 'Hanging is too good for him'; which is an attitude of sheer vengeance. An important practical point in any attempt to abolish the death penalty is the question whether public opinion is firmly wedded to it. The danger has to be reckoned with, that, denied its pound of flesh by the State, the public's passion for retribution would find its outlet in lynching. In a multi-racial community where race crimes generate great waves of hate, this might be a potent argument for its retention. Apart from public emotion, however, the question whether the death penalty is to be retained must be decided on its value as a deterrent.

¹ *Daily Telegraph*, Londen. 10 January 1956.

IMMUNITY AND RESISTANCE IN CLINICAL CANCER*

LIONEL COHEN, M.B., B.Ch., D.M.R.T.

Radiation Therapy Department, Johannesburg General Hospital

In spite of the intensive search for chemotherapeutic remedies, clinical cancer management is, in practice, still limited to surgery and radiotherapy. While both these methods are more or less efficacious in eradicating the primary lesion, and perhaps also the first phalanx of regional spread, most patients so treated still die of disseminated malignant disease. It seems unlikely that the principles of surgical and radiotherapeutic practice could be extended so as to cure those cases for which our current techniques are not adequate. Indeed, far from improving our results, attempts to extend the treated zone frequently diminish the probability of cure. The prognosis seems to be largely determined at the outset by the extent of the tumour at the time of treatment, its rate of growth, and its tendency to metastasize. This suggests that the next important step in the control of clinical cancer is to investigate those factors by which the mammalian host influences the rate of growth and dissemination of tumours.

RESISTANCE IN EXPERIMENTAL CANCER

The history of experimental cancer research is dominated by the rude fact that autogenous growths, including human cancer, will not respond to those simple procedures by which transmitted animal tumours are readily cured. Except under specially controlled conditions, transmitted tumours are genetically and antigenically foreign to their hosts, maintaining a precarious existence in the presence of circulating isoagglutinins.¹ All transplanted tissue, including experimentally transmitted tumours, has been shown to carry specific antigens² which, like the human blood-groups, correspond to definite 'histocompatibility genes'³ in the host. Only in a thoroughly inbred strain of

animals, bearing a tumour which arises regularly in that strain, avoiding prolonged serial passage of the tumour which may permit diversification from its host, can we be reasonably sure of a tumour-stability approaching that operating in human cancer. Otherwise tumour transplants are virtually 'incompatible' with the host, and are easily cured by almost any form of non-specific trauma or intoxication. Almost all chemical agents developed for cancer therapy have been selected on the basis of their non-specific action in mice bearing incompatible tumours and, for this reason alone, cancer chemotherapy as currently practised is unlikely to contribute effectively to human medicine.

On the other hand, a most valuable contribution of animal tumour research to the problem of human cancer lies in the fact that the resistance of the host against its tumour can be modified by many physical, chemical and physiological factors. Murphy⁴ first proved that the reticulo-endothelial system, in particular the lymphocyte, exerts a controlling influence on tumour growth. Agents stimulating the production of antibodies were able to enhance the host's tumour-resistance, often to the point of absolute immunity.⁵ This effect can be evoked by spontaneous regression of unstable tumours,⁶ vaccination with attenuated tumour strains,⁷ injection of non-specific antigens such as embryo skin⁸ which may, however, contain antigens in common with the tumour,⁹ implantation of spleen from normal animals,¹⁰ injection of formaldehyde into the tumour,¹¹ temporary ligation of the blood-supply to the growth,¹² and implantation of radiation-attenuated tumour fragments.¹³ The effect of antisera¹⁴ and of splenic fragments from immune animals¹⁵ was also demonstrated against tumour tissue-cultures *in vitro*. None of these manipulations, however, has conferred a lasting immunity to implants of compatible or autogenous

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tumours, or succeeded in destroying such tumours when established, nor have they had any beneficial effect in human cancer cases.

The converse effect—abrogation of natural or acquired resistance to tumours—is easily produced by factors inhibiting reticulo-endothelial function, such as total body irradiation,¹⁶ blockade of the RE-system with colloids,¹⁷ administration of cortisone and allied drugs,¹⁸ overwhelming doses of antigen in the form of lyophilized tumour,¹⁹ neurogenic stress,²⁰ or local trauma,²¹ irradiation,²² or intoxication.²³ All these agents can promote the onset of tumours, facilitate their growth and dissemination, and inhibit their response to treatment, suggesting that immunological processes might affect the pathogenesis of cancer in man and its prognosis.

IMMUNOLOGICAL MECHANISMS IN THE PATHOGENESIS OF CANCER

The mechanism of immunity must have appeared early in the course of evolution of metazoal organisms, when it became necessary to maintain the integrity of the cell-population by selective elimination of all extraneous cell-types, be they invading parasites or aberrant body-cells. Apparently 'normal' and 'foreign' cells can be distinguished by their characteristic protein structures: genes, enzymes or antigens, which carry identifiable patterns, 'markers'²⁴ or 'information'²⁵ analogous to the cybernetic mechanisms of modern communication theory. Homeostasis can then be maintained by the elimination by the reticulo-endothelial system, through antibodies and phagocytosis, of all cells carrying markers other than those to which the body is adapted. This mechanism resembles the automatic radar defence-system IFF ('identification-friend-foe'), in which friendly craft are fitted with a radar reflection circuit returning a characteristic signal pattern, and the receptors so coded that this pattern alone fails to actuate the defensive missiles. In the vertebrate host the RE-system receives its discrimination-code during foetal life, when it actively acquires a specific tolerance to all antigens present at that time.²⁶ Examples of this effect are found in the human blood-groups, cross-transfusion reactions in dizygotic cattle-twins, intra-uterine grafting experiments, and probably too in the so-called milk-factor of newborn mice. There is, apparently, a critical period in early life before which any proteins present are classified as 'friendly' for future reference, but after which the reaction is reversed and all unrecognized antigens are treated as 'foreign'.

Whether the proximal causation of cancer is a somatic gene-mutation,²⁷ a virus-like transmissible agent,²⁸ or an enzymatic²⁹ or antigenic³⁰ adaptation, is no longer of practical importance, since it now seems probable that these various concepts are merely different facets of the same physical process, initiated either by intrinsic thermodynamic events,³¹ or as a result of endogenous or exogenous chemical or physical agents.³² Cancer cells, whatever their origin, contain genes,³³ antigens³⁴ and enzymes³⁵ other than those found in normal tissue, and are consequently subjected to immunological homeostatic control. For this reason single cancer-cells

or isolated small groups cannot in themselves give rise to malignant tumours, a certain critically large number of cells being required before tumour growth can commence.³⁶

The subcritical dormant tumour-cell colony, however, can suddenly adjust to the presence of antibodies, escaping from homeostatic control, by deleting marker-genes or de-differentiating.³⁷ Multiplication of these mutant cells produces an excess of foreign protein, which will then neutralize circulating antibodies and inhibit their further production.³⁸ In this way an excess of tumour antigen will suppress the resistance of the host sufficiently to permit unrestrained tumour-growth,³⁹ invasion and metastasis.⁴⁰

It would seem to follow that most adults must possess many small groups of isolated neoplastic cells persisting for long periods as 'subcritical colonies',⁴¹ which only occasionally reach critical size and become clinically overt. This situation is recognized in solar hyperkeratoses, small rodent ulcers, intraduct papillomata of the breast, adenomata of thyroid and prostate, intestinal polyposis, and papillomata of the bladder, all of which have been observed in the quiescent 'precancerous' state for many years before active growth supervenes. Presumably a similar phase also occurs in tumours of other less accessible tissues, especially in cases where a precipitating injury such as incomplete excision precedes the overt disease.

There is evidence, too, that the host may continue to exert some restraining influence on the growth of established tumours. A frequent finding at autopsy in cancer cases is the presence of many tumour-cell emboli which have evoked a surrounding inflammatory reaction and are in the process of dissolution.⁴² Similarly, one not infrequently observes a patient who develops distant metastases 15-40 years after removal of the primary growth.⁴³ Apparently tumour-cell emboli can be restrained in a dormant state for extremely long periods, and suddenly become active when the host's resistance is diminished as a result of age, debility or intercurrent disease.

Both, therefore, in the healthy adult carrying subcritical or precancerous foci and in the locally cured patient with subcritical or dormant metastases, those factors which might affect local or systemic resistance are of the first importance in determining future survival. Since these factors are readily influenced by trauma, stress, radio-diagnostic procedures, and medication, they fall within the scope of everyday medical practice.

EXTRANEUS FACTORS INFLUENCING GROWTH AND DISSEMINATION OF CANCER

An almost unlimited range of materials have been shown to induce tumours in experimental animals,⁴⁴ and an equally wide range of common agents to which the human population is habitually exposed in industry,⁴⁵ medical treatment,⁴⁶ social ritual,⁴⁷ and the atmosphere of both town and country,⁴⁸ have been incriminated as probable carcinogens. Carcinogenic agents may, in general, be shown to act in one or more of 3 possible ways:

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1. *Initiating agents* are weakly carcinogenic in themselves but become potent in combination with certain 'promoting' factors.⁴⁹ This group of agents are all effective mutagens, and presumably act through mutation of genetic 'marker' protein, giving a profusion of subcritical tumour-cell foci which, however, can proliferate only if local resistance is suppressed by the action of promoting factors. Examples of this type of action include ionizing radiation, polycyclic hydrocarbons like benzpyrene, and mitotic poisons like triethylene-melamine, which have in common the ability to deliver to the relevant protein molecule a quantum of energy in excess of 3 electron-volts.⁵⁰ Included in this group are many agents with which contact is not easily avoidable, such as the hydrocarbons in smokes, fogs, industrial fumes, pitch, and cigarette tars;^{45,47,48} radiation by cosmic rays, atmospheric radon and uranium dusts, medical and industrial X-rays, and the products of atomic-energy enterprises;⁵¹ and, of special importance in the Transvaal, ultraviolet solar radiation,⁵² to which the skins of all outdoor workers are regularly exposed.

2. *Local promoting factors* or 'co-carcinogens'⁴⁹ are themselves unable to induce cancer, but are very effective in stimulating subcritical precancerous foci into active growth. Almost any form of trauma, chronic irritation, or stimulation of hyperplastic growth, has this effect. Application of croton oil, surgical incision, and injection of foreign material, have all been used experimentally as co-carcinogens.⁴⁹ In the same category are the growth-stimulating hormones, such as oestrogens⁵³ acting on uterine and mammary epithelium, and androgens acting on the respiratory and alimentary tracts, which probably accounts for the sex differences in the susceptibility of these organs to identical carcinogenic stimuli. Promoting factors are of special importance in the management of tumours arising in sites known to harbour other precancerous foci, as in the case of solar hyperkeratosis with skin cancer, or multiple papillomatosis with carcinoma of the bladder. In these cases excision of the primary lesion is often followed by several new primary tumours (sometimes erroneously thought to be recurrences) arising in the surgical scar. In such cases, presumably, a non-traumatic form of treatment without co-carcinogenic effects, such as radiotherapy, might have been preferable. Similarly it is frequently observed that a plastic surgical procedure, which would certainly have been successful for the treatment of skin cancer in, say, an office worker in Europe, means a slow and painful death if indiscriminately applied to a Transvaal farmer or bricklayer.

3. *Systemic promoting factors* comprise that large group of agents which inhibit immunological mechanisms. They include injection of colloidal materials which mechanically blockade the RE-system, such as india-ink, trypan-blue, ferric saccharate (recently marketed for intravenous iron medication), and thorium dioxide sol (radiodiagnostic contrast medium);⁵⁴ agents producing lymphopenia, such as total body radiation⁵⁵ and virus infections like influenza;⁵⁶ mitotic poisons and similar drugs used for cancer palliation, including mustard-gas derivatives, folic acid, purine and amino-acid antagonists (aminopterin, azoguanine, and sarco-

lysine), and synthetic vitamin-K analogues (menadione or 'synkavit');⁵⁷ excessive doses of anti-reticular cytotoxic sera;⁵⁸ hormones, like pituitary corticotrophin and possibly certain adrenal steroids;⁵⁹ and all severe injuries, debilitating illnesses, pregnancy, and major surgical procedures, collectively classified as 'stressors'.⁶⁰ Although many of these agents have been observed to inhibit temporarily the growth of established tumours—hence their repute as palliative agents—they tend, in general, eventually to accelerate tumour proliferation and dissemination.⁶¹

The 3 levels of carcinogenic action described are not entirely independent categories, and some of the agents enumerated may work at more than one level. Powerful carcinogens like methylcholanthrene and radio-active materials, for example, are known to act at all 3 levels, others apparently at 2, and many behave more or less in the manner indicated. From the practical point of view, it is the obvious duty of every physician to prevent, as far as possible, the onset of cancer by minimizing exposure to suspected or potential carcinogenic agents, eliminating all inessential diagnostic radiographic examinations in younger members of the community, avoiding all forms of radiotherapy or administration of radio-active isotopes for non-malignant conditions unless a serious threat to life or health makes such exposure essential, ensuring adequate protection of the community from radio-active products, including atmospheric and oceanic contamination by atomic bombs, discouraging smoking and similar suspect habits, and urging control of smoke, soot, and motor exhaust fumes. The older members of the community, who presumably already carry precancerous foci, and in particular apparently-cured cancer cases who may carry dormant tumour-cell rests, should especially not be exposed to promoting factors such as corticotrophic, gonadotrophic and sex hormones, any of the cancer-palliative drugs known at present, avoidable trauma, and stress-inducing operations, although chronic irritative or inflammatory conditions should be corrected. Many of the drugs mentioned are useful in the palliation of incurable malignant disease, but it is obviously important to avoid their use in curable cases, even long after the tumour has apparently been eradicated.

HOST RESISTANCE AND THE RESPONSE TO THERAPY

The significance of systemic immunity in clinical cancer control is nowhere better illustrated than in the response of tumours to radiation. The doses used clinically are known to have little direct effect on the tumour cells *per se*, and doses from 10 to 100 times greater are found necessary to destroy cancer cells irradiated outside the host in tissue culture.⁶² A tumour irradiated *in situ*, however, undergoes a subtle antigenic change rendering it susceptible to immunological and phagocytic processes in the host, which can then effect its destruction. Any factor tending to isolate the tumour from the vascular and cellular elements in its bed will prevent its regression following otherwise on adequate irradiation.⁶³ Tumours in avascular scars and ulcers, particularly the devitalized scars and necrotic ulcers from previous irradiation, are notoriously radio-

resistant. Similarly factors inhibiting systemic immunity, such as total body irradiation or mitotic poisons, including cortisone and other cancer-palliative drugs like nitrogen mustard and azoguanine, will all render tumours incurable by radiotherapy.⁶⁴ Even the so-called radiosensitizing agents such as menadione or 'synkavit' will in fact prevent complete regression of adequately irradiated tumours.⁶⁵ It would seem that practically all palliative procedures automatically preclude the possibility of cure.

Further, when extensive or deep-seated tumours are irradiated, the correspondingly large volume-dose itself induces a leukopenia and inhibits reticulo-endothelial function, with the result that such tumours often fail to respond to ordinarily curative doses. The systemic resistance factor thus sets the upper limit for size and depth of tumours curable by conventional radiotherapy.

The converse of this effect, that is the enhanced radiosensitivity of tumours when host-resistance is stimulated, has only recently been demonstrated with homozygous tumours grown in genetically modified heterozygous hosts,⁶⁶ with a mutant tumour grown in homozygous hosts, and with tumours grown in hosts specifically immunized against them.⁶⁷ These effects point to the future possibility of specifically immunizing the human host against his own tumour, thus enhancing its curability by radiation and possibly also preventing or delaying the growth of metastases.

CLINICAL EFFECTS OF ENHANCED TUMOUR RESISTANCE

The response which might be expected were it possible to enhance the patient's resistance to his tumour, is exemplified by those rare cases when the tumour is genetically or antigenically distinct from the normal tissues. The testicular seminoma, for example, arising from haploid germ-cells in a diploid host, is the most radiosensitive human tumour known and can be cured by radiation even when widely disseminated.⁶⁸ Another example, the chorionepithelioma, arising from foetal cells and growing in the maternal host, is exceptional in that, even in the presence of metastases, it frequently regresses spontaneously after removal of the primarily affected organ.⁶⁹

All too rarely one encounters in the follow-up clinic a patient who, owing to some obscure and fortuitous combination of circumstances, develops an unusually effective resistance against his tumour.

Case 1. Miss W., a 60-year-old European spinster, presented at the Johannesburg Hospital in 1948 with a Stage-II carcinoma of the upper outer quadrant of the right breast of 9 months' duration. The primary growth was 7 cm. in diameter, not attached to deeper structures, but there was an enlarged hard mobile lymph-node in the right axilla. She was treated by radical mastectomy and routine post-operative roentgen therapy. Histologically the tumour was a high-grade, rapidly proliferating, spheroidal-celled carcinoma. In 1950 the patient developed widely-dispersed skin metastases over the whole trunk, head and neck. Although no treatment was necessary, the patient being free of symptoms and having what was considered a hopeless prognosis, some of these skin nodules were irradiated experimentally, purely in order to corroborate the minimum lethal dose after Friedman's method.⁷⁰ Using small fields of superficial radiation, 24 separate nodules were given a series of successively smaller single doses over a period of 4 years. Of the 24 nodules treated, 17 disappeared completely after doses ranging from 2000 r down to as low as

300 r. Since the lethal dose of the average breast-cancer and its satellite nodules, under the physical conditions used here, is not less than 1200 r,⁷⁰ this result indicates a greatly increased radiosensitivity. Nodules given 250 r or less or left untreated, reached a size of 10-15 mm. in diameter and then remained stationary for the 5-year observation period (Fig. 1). Biopsy of one such stationary nodule showed the same high-grade, rapidly growing,

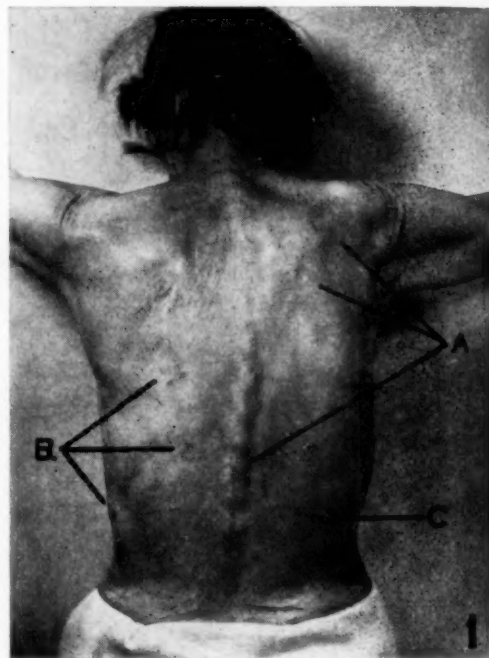


Fig. 1. Metastatic cutaneous carcinomatosis, showing, (A) nodules cured by moderate dosage ranging from 500-2000 r in a single exposure, (B) nodules persisting unchanged after doses of 200-300 r, and (C) untreated nodule remained static for a 5-year observation period.

spheroidal-celled carcinoma as the primary growth. The patient has remained symptom-free without any further extension of the tumour, and except for poor nitrogen balance, has remained physically healthy for 8 years after the onset, and 5 years after overt dissemination of her tumour. As in the experimental animals, a markedly increased radiosensitivity is here associated with a degree of anti-tumour resistance in the host. Whether this resistance was built up by irradiation of the series of small deposits with progressively diminishing doses, or whether the patient had the good fortune to possess a strong tumour resistance *ab initio*, is a matter for future investigation.

Apart from systemic immunity, the effect of local resistance on the growth of metastatic tumour is well-illustrated by

Case 2. Mr. L., a 59-year-old European mechanic, presented at the hospital in 1948 with a 6-cm. diameter squamous carcinoma of the dorsum of the left hand of 2 years' duration. This was treated with superficial radiotherapy. Seven months later there was an obvious local recurrence, and involvement of the epitrochlear and axillary lymph-nodes. All three sites showed squamous carcinoma on biopsy, and were treated by intensive irradiation. For the succeeding 6 months the patient was well except for a small necrotic ulcer at the primary site. He then suddenly developed a febrile constitutional reaction with a generalized macular

rash. The skin rash faded within a few days, except for those lesions inside the irradiated areas which persisted and increased. Some weeks later each macule within the irradiated skin-fields



Fig. 2. Metastatic cutaneous melanomatosis confined to two irradiated axillary skin fields. There is obviously a resistance-factor operating in the unaffected skin.

had developed into a palpable tumour. The lesions became confluent, forming two rectangular tumour-masses exactly demarcating both axillary treatment-fields (Fig. 2). Biopsy of these lesions showed unpigmented malignant melanoma! Although the primary melanoma was not found, the patient dying shortly afterwards without necropsy, there can be no doubt that widespread melanoma-cell embolization had occurred, but that all tumour emboli were effectively suppressed except in those tissues where local resistance had been impaired.

CONCLUSIONS

Both local and systemic tumour-resistance factors have been identified in the human being, shown to determine the appearance of certain tumours, and to affect profoundly the prognosis of treated cancer. It behoves the physician to remain aware of these effects, particularly in relation to the existence of precancerous or sub-clinical tumour-foci, and to avoid local trauma, stress-inducing manipulations or medication which might embarrass the resistance mechanism and thus promote the onset of overt cancer.

In the management of established growths it is essential to decide at the outset between palliative and curative treatment, since all palliative therapy or medication interferes with local or systemic resistance-factors and thus precludes cure.

Follow-up of successfully-treated cancer cases also requires special care in avoiding procedures which may release residual tumour-rests from the local restraint

imposed by cellular or fibrous reactions, and avoiding traumatic or surgical stress, use of cancer-palliative drugs, or administration of growth-stimulating hormones, all of which may possibly activate dormant metastatic deposits.

The converse of these processes, i.e. immunologically-induced sensitization of the tumour, has been shown to be feasible, at least in one experimental species, and would, if applicable to humans, probably result in increased radiocurability of the tumour and delayed onset of recurrence or metastasis in the partially controlled case.

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UNION DEPARTMENT OF HEALTH BULLETIN

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Plague, Smallpox, Typhus Fever: Nil.
Epidemic Diseases in Other Countries.
Plague: Nil.

Cholera in Dacca (Pakistan).

Smallpox in Rangoon (Burma); Phnom-Penh (Cambodia); Ahmedabad, Allahabad, Bombay, Delhi, Kanpur, Madras, Nagpur (India); Dacca (Pakistan); Hué (Viêt-Nam).
Typhus Fever: Nil.

ENDOKRIEN-FAKTORE BY ACNE VULGARIS S. JUVENILIS*

R. KOOLJ, M.D. (AMSTERDAM)

Huidarts. Navorsingsbeampste, Westfort-Inrigting, Unie-Departement van Gesondheid, Pretoria

Dit is 'n bekende feit dat acne meestal omstreeks die puberteitsjare ontstaan. Vandaar dan ook die naam acne juvenilis. Die ou Grieke het die siekte Jonthos genoem, wat letterlik jongeling, of eerste baardhare, beteken. Oor die herkoms van die woord 'acne' heers daar nog verskil van opvatting; sommige meen dat dit 'n verbastering of skryffout van die Griekse woord 'Acme' is, wat volbloei, of ontwikkeling van die sisteem, beteken. Hieruit blyk dat dit reeds opgemerk was dat acne in verband staan met die puberteitsjare van die individu.

Acne vulgaris word nie deur 'n bepaalde letsels gekenmerk nie. Dit toon 'n polimorfe beeld. By 'n ten volle ontwikkelde siektebeeld kry ons komedone, follikulêre papels en pustels wat vlak of diep geleë mag wees, asook absesse, rofies en littekens. Dan praat ons van acne polimorfa. Die leeftyd waarop acne vulgaris begin en op welke leeftyd dit die meeste voorkom is noukeurig en uitvoerig deur Bloch¹ te Zürich nagegaan. Die eerste komedone (tot 20) het hy reeds op 76-jarige leeftyd gesien, respektiewelik in 13 persent en 32 persent by albei geslagte. Die frekwensie neem toe met die styging

in leeftyd en bereik die maksimum by meisies op die 17de jaar (80 persent) en by seuns reeds op 13-jarige leeftyd (71 persent). Daar het meer ernstige vorms by seuns voorgekom as by dogters. Hinrichsen en Ivy² het in Chicago 'n soortgelyke ondersoek verrig. Hulle resultate kom in breë trekke ooreen met dié van Bloch. In teenstelling met Bloch, vind hulle egter dat acne by seuns later begin en dat ook die ernstige vorms op latere leeftyd ontstaan. Moontlik is ras, klimaat en dergelike faktore hiervoor verantwoordelik.

Enkele gevalle van acne by pasgebore (acne neonatorum) en by klein kindertjies (acne infantilis) is ook beskrywe. Soms blyk dit dat daar 'n biniertumor of 'n ander endokrien-stoornis bestaan, gewoonlik egter word daar geen afwykings gevind nie, en dan verdwyn die aandoening na 'n tyd gewoonlik spontaan. Acne kan ook eers na die puberteit begin; dit is meestal hardnekkige vorms.

Acne en Endokrien Faktore. Behalwe die veelvuldige voorkoms van acne in die puberteit toon ook die volgende feite op 'n verband tussen die ontstaan van acne vulgaris en endokrien-faktore.

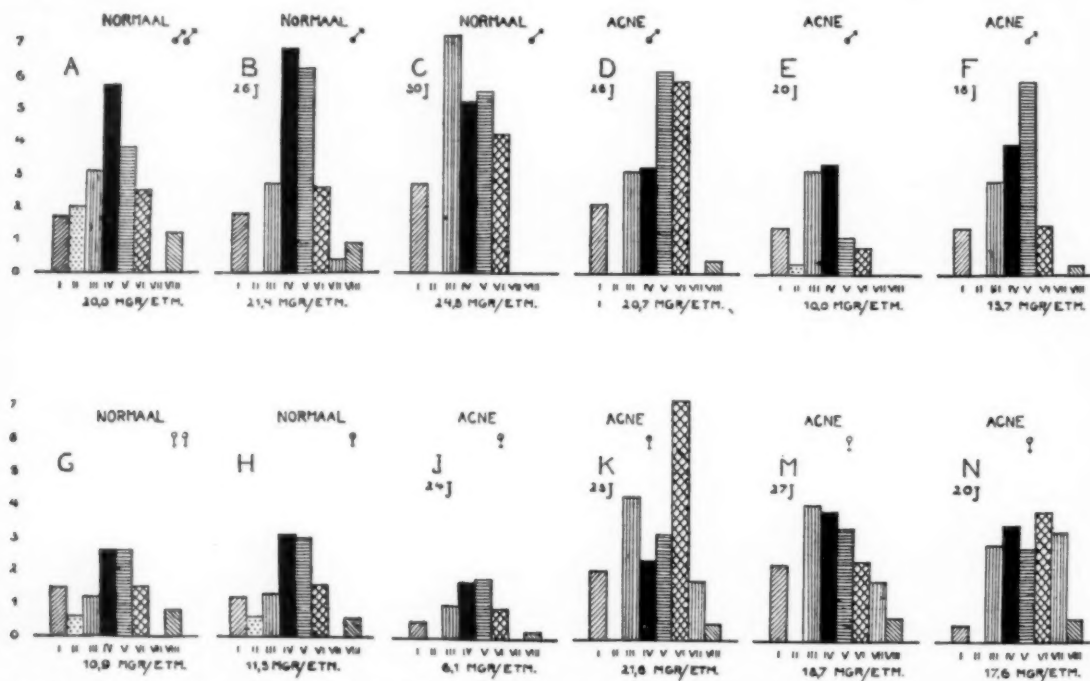


Fig. 1. Diagram 17-Ketosterioïede. I. Artefakte. II. I-Androstanolon. III. B-ketosterioïede. IV. Androsteron. V. Aetiocholanolon. VI. 11-Ketoetiocholanolon + 11-Hydroxyandrosteron. VII. 11-Hydroxyandrosteron. VIII. Nie-geïdentifiseerde 17-ketosterioïede.

* 'n Referaat ingedien op die Suid-Afrikaanse Mediese Kongres te Pretoria, Oktober 1955.

1. Acne kom dikwels voor by pasiënte met hiper-gonadisme, bepaalde byniertumors en soms by pasiënte met 'n Cushing-sindroom.

2. Acne is waargeneem by pasiënte wat met ACTH (en cortisone?) behandel is (Brunner *et al.*³).

3. Acne kom nie voor by klein kindertjies nie behalwe in die bogenoemde uitsonderingsgevalle.

4. Acne kom nie voor by kastrate en eunuchs nie.

5. Behandeling van kastrate en eunuchs met testosteroon propionaat verwek in die meeste gevalle acne wat weer verdwyn na die staking met die behandeling (Hamilton⁴).

6. Acne verminder of verdwyn in die reël tydens swangerskap.

7. By vroue word dikwels 'n verergering van die acne waargeneem omstreeks die tyd van menstruasie.

Acne en Talgkliersekresie. Dit is 'n algemeen bekende feit dat acne vulgaris by pasiënte dikwels gepaard gaan met vermeerderde talgkliersekresie (seborrhoea). Dit is dan ook aanneemlik dat 'n vermeerderde en moontlik ook 'n veranderde talgkliersekresie van etiologiese betekenis is by acne vulgaris. Brunner *et al.*³ veronderstel dat die sebum by acne-pasiënte vinniger hard word, waardeur die follikelopening maklik verstopt. Hierdie proses word nog verhaas deur die hiperkeratose van die haarfollikel by acne.

Eksperimentele Gegewens. Verdere steun vir die bogenoemde opvatting kan verkry word uit resente eksperimentele gegewens by mense en diere oor die hormonale regulering van talgkliere. Androgeen-stowwe vergroot die talgkliere, terwyl hulle deur die estrogeen-stowwe kleiner word (de Graaf,⁵ Ebling,⁶ Pfeiffer,⁷ Rony en Zakon,⁸ en Lapière.⁹ Hamilton en Montagna¹⁰ het histochemies aangetoon dat androgeen-stowwe aan hamsters toegedien die samestelling van die sebum verander. Aron-Brunetiere¹¹ en Haskin *et al.*¹² het aangetoon dat progesteron die talgkliere van diere aansienlik vergroot. Laasgenoemde ondersoekers het 'n positiewe invloed van ACTH op die talgkliere aangetoon. Die invloed van kortisone was nie duidelik nie. Lasher, Lorincz en Rothman¹³ het aangetoon dat een of ander hipofise-faktor nodig is vir die instandhou van die talgkliere.

Hormoonbepaling by Pasiënte. Daar is ook getrag om deur bepaling van estrogeen- en androgeen-stowwe in die urine van lyers aan acne vulgaris aanduidings te vind van 'n hormonale stoornis. Dit is oor die algemeen 'n baie tydrowende ondersoek. Die resultate van sodanige ondersoek soos in die letterkunde vermeld is nogal teenstrydig. 'n Verlaging van die estrogeen-stowwe in die urine van pasiënte met acne vulgaris het die meeste voorgekom. Vir literatuur en nadere besonderhede word verwys na 'n artikel oor hierdie onderwerp deur die skrywer hiervan en medewerkers.¹⁴ Die resultate van hierdie ondersoek word hier kortliks meegedeel. By 30 mans met 'n hardnekkige vorm van acne vulgaris en by 21 normale mans (18-37 jaar) is die gehalte van die 17 ketosteroïede en meestal ook van die estrogeen-stowwe in die urine bepaal. Geen verskille is gevind nie (Tabel I). Die estrogeen-stowwe is biologies bepaal op die estrus van gekasteerde vroulike muise (Allen-Doisy-

TABEL I. GEGEWENS BETREFFENDE 21 BEPALINGS BY NORMALE MANS EN 30 BEPALINGS BY MANS MET ACNE VULGARIS

Leeftyd	17 K.S. Pmg./24 u	Oestr. stowwe I E./24 u Normaal	Quotient 17 K.S. oestr. stowwe
18	16.7	110	0.15
18	28.7	100	0.29
18	12.5	120	0.10
20	14.2	150	0.095
21	14.1	70	0.20
22	12.5	125	0.10
23	9.9	100	0.10
24	17.6	50	0.35
24	27.2	300	0.09
25	11.6	140	0.08
25	14.6	110	0.13
26	16.4	150	0.11
26	25.0	120	0.21
27	13.4	100	0.13
27	12.1	40	0.30
28	12.7	110	0.115
30	17.9	50	0.36
30	24.1	95	0.25
31	31.3	45	0.70
35	19.6	55	0.36
36	19.6	90	0.22
18-36	17.7	106	0.21
Acne			
18	13.1	65	0.20
19	11.8	150	0.08
20	8.3	100	0.08
20	16.4	260	0.06
20	14.0	50	0.28
21	17.6	100	0.18
21	18.0	50	0.36
21	10.5	80	0.13
21	13.8	45	0.31
21	17.2	60	0.29
22	16.6	60	0.28
22	11.2	35	0.32
22	19.5	300	0.065
22	16.1	75	0.21
22	16.1	125	0.13
23	13.8	300	0.05
23	21.5	140	0.15
24	22.4	85	0.26
25	30.0	150	0.20
25	18.2	120	0.15
26	19.3	40	0.48
26	22.7	540	0.04
26	13.3	75	0.18
26	19.1	150	0.13
28	21.8	100	0.22
28	14.1	65	0.22
29	20.8	105	0.20
33	13.9	110	0.13
35	16.8	—	—
35	18.4	170	0.11
18-35	16.9	128	0.19

metode) en die 17 ketosteroïede is kolorimetries bepaal (volgens Dingemanse, Callow en Fraser). Ook is geen verskille vir die uitskeiding van 17-ketosteroïede by 18 vroue met acne vulgaris gevind nie in vergelyking met dié van 21 normale vroue (Tabel II). Hoewel die afwesigheid van verskille in uitskeiding van estrogeen- en androgeen-stowwe by pasiënte met acne vulgaris nie 'n stoornis op hierdie gebied uitsluit nie, kan dit tog daarop wys dat daar waarskynlik nog ander hormone van

TABEL II. GEHALTE VAN URINE AAN 17-KETOSTEROÏDE, BEPAAL BY NORMALE VROUENS EN VROUENS MET ACNE VULGARIS

Normaal			Acne		
Leeftyd	16 K.S. mg./24 uur		Leeftyd	17 K.S. mg./24 uur	
18	7.7		19	10.2	
19	16.1		20	10.5	
20	8.0		20	10.6	
20	10.2		20	8.8	
21	13.0		21	9.6	
23	11.2		22	9.4	
23	17.6		22	11.8	
23	4.8		22	13.4	
25	13.0		22	14.7	
28	14.2		23	9.1	
28	15.0		24	8.4	
30	7.9		25	21.5	
30	9.0		26	15.0	
30	13.6		27	10.7	
30	16.6		30	12.5	
30	6.0		32	13.9	
32	15.9		36	24.7	
33	14.7		36	12.7	
34	5.5				
37	12.1		19-36 ..	12.6	
38	5.8				
18-38 ..	11.3				

etiologiese betekenis by acne is. 'n Aanduiding hiervan kan gesien word in die resultate van die bepalinge van



Fig. 2. Talgklier van 'n gehipofisektomeerde en gekastreerde rot. Onbehandel.

die 17-ketosteroïede-mengsel wat ons by 7 acne pasiënte gevind het (Fig. 1). By 4 pasiënte was die resultate in die rigting van 'n verhoging van bynierskorsaktiwiteit. Dit moet egter nog verder bevestig word.

Proewe op Diere. De Graaf en Kooij¹⁵ het die invloed van ACTH op die talgkliere van gehipofisektomeerde en gekastreerde rotte ondersoek. Die talgkliere was na behandeling met ACTH matig vergroot in vergelyking met dié van die kontrole-rotte (Figs. 2 en 3). 'n Mens

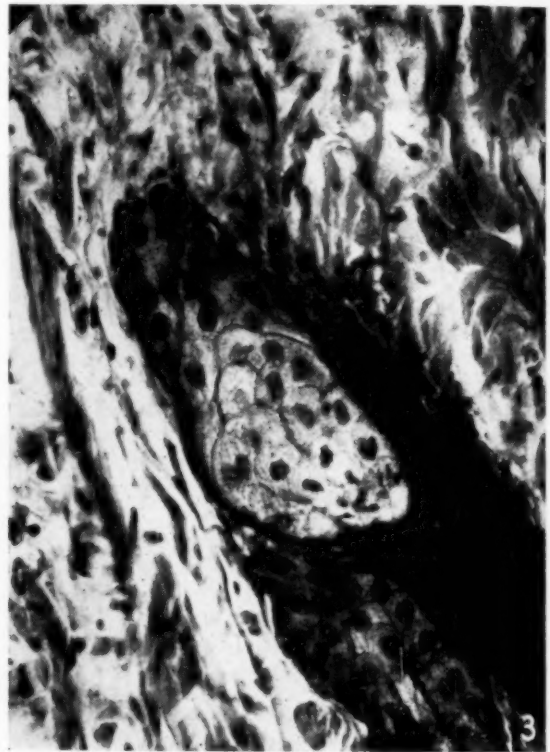


Fig. 3. Talgklier van 'n gehipofisektomeerde en gekastreerde rot behandel met ACTH.

is geneig om hierdie vergroting aan androgeen-bynierskorsstowwe toe te skrywe. Hierteen pleit die feit dat die saadblasies van sodanig behandelde rotte nie vergroot was nie. Die byniere het egter deur die behandeling swaarder geword, waarvan afgelei kan word dat die ACTH werksaam was. Ook op andere maniere kan ons aantoon dat dit onwaarskynlik is dat die ACTH via produksie van androgeen-stowwe uit die bynier op die talgkliere gewerk het. Kortheidshalwe word hier nie verder op ingegaan nie. Moontlik berus die effek op 'n nog onbekende nie-androgene invloed van die bynier. Dat die hipofise van belang is vir die talgklier blyk uit die Figs. 4 en 5; Fig. 4 toon 'n beeld van die talgklier van 'n onbehandelde gehipofisektomeerde rot; Fig. 5 van 'n gehipofisektomeerde rot wat behandel is met 'n hormoon wat 'n hipofisewerking het.



Fig. 4. Talgklier van 'n onbehandelde gehipofisektomeerde rot.



Fig. 5. Talgklier van 'n gehipofisektomeerde rot behandel met hormoon met 'n hypofise werking.

Kommentaar en Konklusies. Uit die bostaande kan myns insiens besluit word dat endokrien-faktore van etiologiese betekenis by acne vulgaris kan wees. Behalwe endokrien-faktore is ook ander, soos voeding, stofwisseling, infeksies, emosie (eksamens), 'stress' (Selye) en die besondere gevoeligheid van die weefsel, wat die ontstaan van acne beïnvloed. Acne vulgaris het 'n multi-kousale of beter nog 'n multikondisionele genese. Wat die hormonale faktore betref, lyk dit aanneemlik dat 'n absolute of relatiewe oorheersing van androgeen- oor estrogeen-hormone in die liggaam die ontstaan van acne kan bevorder. Hipofise- en bynierskorshormone egter, en by die vrou, die progesteron kan dit waarskynlik ook bevorder. So kan 'n stoornis in die ingewikkelde samespel van die hormone acne verwek. Volgens de Jongh¹⁶ begin die ovarium van jong dogters met die produksie van androgeen-stowwe sonder dat dit voldoende deur estrogeen-stowwe gekompenseer word. Dit sou die veelvuldige voorkoms van acne by meisies op hierdie leeftyd verklaar.

BEHANDELING

Dit is begryplik dat daar getrag is om acne vulgaris met behulp van hormone te behandel. Daar moet egter onthou word dat die toegediende hormoon nie net op die talgklier werk nie dog op die hele organisme, en dat

dit op dié wyse die werking van die ander organe soms nadelig kan beïnvloed. Hormoonbehandeling kom myns insiens dan ook alleen vir hardnekkige gevalle van acne in aanmerking. 'n Ander moeilikheid is dat 'n mens in die meeste gevalle nie weet of daar 'n endokrien-stoornis bestaan nie en nog minder watter hormone versteur is. Die ingewikkelde en tydrawende hormoonbepalings kan in die meeste gevalle nie gedoen word nie. Wat die manier van toediening van die hormone betref, moet die lokale applikasie die voorkeur kry. Daar moet egter onthou word dat, veral by die langdurige lokale toediening van hormone, daar resorpsie in die liggaam plaasvind. Gunstige resultate word beskrywe van die lokale toediening van estrogene stowwe by acne vulgaris. Ook word mondelike en parenterale toediening van natuurlike en sintetiese estrogeen-stowwe by hierdie siekte gebruik. Jarrett¹⁷ het na mondelike toediening van 3 mgr. stilboestrol per dag vermindering van die sebum op die veloppervlakte en verbetering van die acne waargeneem. Hy ag dit ook moontlik dat oestrogeen-stowwe die sebum kwalitatief verander.

Aron-Brunetiere¹¹ beveel inspuitings of liefs implantasie van gonadotroophormone aan. Dit skyn asof kortisone 'n gunstige uitwerking kan hê op acne vulgaris (Didot¹⁸). Dit is in teenstelling met vroeëre mededelings waarin beskrywe is dat kortisone juis acne kon veroor-

saak (Brunner *et al.*³). 'n Gunstige uitwerking kan verklaar word deurdat kortisone die produksie van androgeen-stowwe in die bynier rem.

Waar daar opvlamming van acne beskrywe word deur hoë dosisse progesteron, word daar van lae dosering gunstige resultate vermeld. Dit kan verklaar word deur 'n bifasiese werking, wat meer by hormoonwerkinge waargeneem word. Verder moet by die beoordeling van die terapeutiese resultate by pasiënte met acne vulgaris onthou word dat die verloop van die siekte baie veranderlik is; 'Spontane' beterskap en verergering (menstruasie!) kom dikwels voor. Vir 'n presiese waardebeoordeling van 'n geneesmiddel vir acne vulgaris is dan ook 'n groot aantal pasiënte nodig en 'n kontrole-reeks wat met 'n plasebo behandel word. Voordat egter tot hormonale behandeling oorgegaan word, moet getrag word om deur uitwendige behandeling, diëet en die voorskrywe van 'n bepaalde leefwyse die acne te 'genees'. Met behulp van uitwendige behandeling kan die hiperkeratose, die seborrheea en die infeksie bestry word. Swawel word oor die algemeen hiervoor gebruik, bv. lotio Kummerfeld (sulf. praec. 5-15% camph. 30, mucil. gummiarab. 10-0, Sol. Hydrat. calc. 134-0 Aq. rosae 133-0). Dit word saans op die vel gepenseel, nadat die vel vooraf met water en seep gewas is. As daar op hierdie manier nie voldoende afskilfering plaasvind om die verstopping van die follikel op te hef nie, dan kan ac. salicylicum of (en) resorcine in stygende konsentrasies by die middel gevoeg word. Ook kan afskilfering van die vel verkry word deur bestraling met die hoogteson. Aandag moet gegee word aan stoornisse van die maag-dermkanaal (konstipasie) en aan die diëet. Daar moet gewaarsku word teen die oormatige gebruik van vette en koolhidrate. Veral vark-produkte, melk, room, neute en sjokolade word as skadelik beskou, maar daar is ook groot individuele verskille.

Hardnekkige infeksies kan met die moderne chemoterapeutiese en antibiotiese middels bestry word, dog hul moet nie te ligvaardig gebruik word nie. Teen die lokale toediening van sulfapreparate moet met nadruk gewaarsku word weens die gevaar van sensitiwiteit (Kooij en medewerkers¹⁹). Daar is verskil van mening omtrent die waarde van vitamine A by acne vulgaris. Germeraad²⁰ het wel aangetoon dat baie hoë dosisse vitamine A by acne werkbaar is. Ten slotte moet nog gewys word op die gunstige resultate wat met Röntgen- en Bucky-strale verkry kan word. Hierdie behandeling word egter ook gehou vir die hardnekkige gevalle.

Daar moenie lig gedink word oor acne vulgaris as siekte nie. Hoewel die lewe nie daardeur bedreig word nie kan dit wel daardeur bederf word. Deur die lokalisasie in die gesig ontstiet dit die uiterlike waardeur die pasiënt baie moeikhede kan ondervind. Dit is dikwels 'n rede vir afwysing by aansoek om betrekking en bemoeilik die huwelikskanse. Die pasiënte word sku en kry 'n minderwaardigheidskompleks. Acne vulgaris kan 'n groot psigiese trauma by pasiënte wees. Lyers aan hierdie siekte verdien dan ook die grootste aandag en sorg van die medikus.

OPSOMMING

'n Kritiese oorsig word gegee oor die betekenis van endokrien-faktore vir die ontstaan van acne vulgaris. 'n Verband tussen die ontstaan van acne vulgaris en 'n verhoogde en moontlik kwalitatief veranderde talgklier-sekresie word aanneemlik geag. Die invloed van hormone op die talgkliere van diere word aangetoon aan die hand van persoonlike ondersoek sowel as van andere. Die resultate van hormoonbepalings in die urine van pasiënte met acne vulgaris word bespreek, sowel as die fisiologiese en patologiese toestande by persone wat aandui op 'n verband tussen endokrien-faktore en acne vulgaris.

Ten slotte word aanwysings gegee vir die behandeling van pasiënte met acne vulgaris.

SUMMARY

A critical review is given of the aetiological significance of endocrine factors in acne vulgaris. It is assumed that a relation exists between acne vulgaris and an increased and probably qualitatively altered secretion of the sebaceous glands. The influence of hormones on the sebaceous glands is demonstrated from personal and other investigations.

The results of hormone estimations in the urine of patients with acne vulgaris are reported. Furthermore physiological and pathological conditions are mentioned in man which point to a relation between endocrine factors and acne vulgaris.

Finally indications are given for treatment.

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THE MANAGEMENT OF CARCINOMA OF THE MOUTH*

T. SCHRIRE, F.R.C.S.

Surgeon, Groote Schuur Hospital, Cape Town

The surgical treatment of carcinoma of the mouth enjoyed a certain popularity between 1880 and 1905. During this period many of the hazards peculiar to operations in this area were discovered. Anaesthetic difficulties, the uncontrolled spread of infection, and the problems of maintaining proper nutrition after operation, led surgeons to abandon this form of treatment. The discovery of radium by Röntgen and Becquerel, and the personal experience by the latter of the caustic effects of radium and its salts, were quickly followed by investigation on the selective response of tumour cells to gamma rays. It was with great relief that the surgical world gave up its unrewarded efforts on carcinoma of the mouth, and the cases were gladly turned over to the radiotherapists for their attention.

During the last 45 years a large amount of work has been done, and an immense volume of evidence has accumulated. Unfortunately the universal hope that in radiotherapy we had a panacea for growths in the mouth has not been fulfilled and we are coming more and more to recognize the limitations and contra-indications of this form of treatment.

Within the last few years the tremendous strides made by anaesthesia have enabled the surgeon to attack areas which under earlier conditions were impossible to approach. A far better understanding of the fluid, electrolyte and protein requirements of the body has enabled us to deal with a fair degree of precision with the post-operative difficulties in patients to whom the ordinary methods of feeding are not available.

The immense benefits conferred by the development of antibiotics in preventing infection under the most difficult circumstances, and the solid and massive support of plastic surgery have also enabled the surgeon to tackle with resolution cases which were previously considered inoperable. He can now deal with carcinoma of the mouth in a radical way, confidently anticipating that, with the cooperation of the plastic surgeons, there would be very few surgical mutilations that could not be rendered comfortable and tolerable both to the patient and to his relations.

INDICATIONS FOR SURGERY

The limits of radiotherapy have long been recognized and it is now possible to define these limits with a fair degree of accuracy. It is well known that all tumours are not equally radio-sensitive and that some do not respond to radiotherapy in the ordinary way. Anatomical difficulties, which prevent uniform calculated doses from being given are often present. In addition, glandular metastases and bony involvement have long been rightly regarded as radio-resistant. The following are the indications for surgery:

1. Where the primary tumour is radio-resistant.

* A paper presented at the South African Medical Congress, Pretoria, October 1955.

2. Where the anatomical situation is such that accurate radiation dosage is difficult.

3. Where radiotherapy has arrested the disease incompletely.

4. Where glandular involvement has occurred.

5. Where bone has become involved by carcinoma.

6. In Coloured and Native patients.

1. *The Primary Tumour is Radio-resistant*

Certain tumours in the mouth show greater radio-resistance than others. Why it should be so is not known, and the ordinary methods of histological examination do not give us any indication which tumour is going to be radio-resistant. In many instances, only the failure of an adequately planned dose of radiotherapy will show the nature of the individual malignancy. However, anaplasia which can be recognized histologically, is usually considered an indication that the cancer is radio-sensitive; anaplastic tumours form 7% of our series.

2. *Anatomical Difficulties*

Failure of radiotherapy is something that can often be anticipated. The anatomical position of the tumour may be such that it may be very difficult to arrange for the beams to be directed with accuracy; the extreme mobility of the parts make the calculation for radium or radon seed implantation, and the actual implantation itself, a very difficult and occasionally haphazard procedure.

Because of these difficulties, the dosage received by some tumours cannot be estimated with accuracy and the response is not expected to be satisfactory. As a result of bitter experience most radiotherapists are able to recognize those cases which will be difficult as soon as they encounter them.

3. *Recurrence after Radiotherapy*

The radiotherapist can have only one chance of curing the disease. Should cure not be complete—and by cure one means complete resolution of the process with the absence of any residual ulceration or nodularity—we must conclude that radiotherapy has not succeeded. A second course of treatment is extremely dangerous and will often lead to massive and unpredictable necrosis with the disease still uncontrolled. These cases are pre-eminently candidates for surgical intervention.

4. *Glandular Involvement*

Once glands have become invaded with squamous carcinoma, some alteration takes place either in the radio-sensitiveness of the tumour cell or in its environment and radiotherapy becomes less effective. This has long been recognized and surgical excision of secondary glands has been practised in some clinics for many years.

5. *Involvement of Bone*

Certain cancers by virtue of their anatomical situation always involve bone by the time they are diagnosed. Of these tumours the alveolar carcinomata are the com-

monest and, as they originate in the mucous membrane covering the mandible or maxilla, they invade the Haversian systems very quickly. Sometimes these tumours are observed when an extracted tooth fails to heal and it should be widely known that whenever unexplainable delay occurs in the healing of a socket a snip should be taken for biopsy. Tumours of the hard palate likewise rapidly invade the bone and for that reason it has become our practice to advise operation in these two forms of carcinoma of the mouth as soon as the diagnosis is established.

Involvement of the mandible by carcinoma extending from the floor of the mouth and from the side of the tongue often takes place. It is important to realise, however, that not all apparently fixed epitheliomata have actually invaded the bone; a large proportion are attached by an inflammatory reaction only. The differentiation between the two, though difficult, is occasionally possible and may permit a patient to avoid an operation and receive radiotherapy or, if an operation be mandatory, to save the bone.

6. Coloured and Native Patients

A careful study of the records at our disposal shows that, regardless of the state of the tumour, of its duration or of its histological character, the proportion of radiotherapeutic successes in non-European patients is so low that one can no longer justify this form of treatment in patients of these races.* On the other hand, our only long-term survivals in Coloured and Native patients have been those cases that have been subjected to extensive surgery at the earliest opportunity. The survival rates in patients treated in this way compares very well with those in Europeans similarly treated, and we have found that the non-Europeans stand up well to surgery and to the unavoidable mutilation that is occasionally necessary.

ETIOLOGY

In cancer of the lip we have found a very close relationship between exposure to sunlight and the disease, but cancer of the mouth has not, in our experience, been associated with any specific disease. It is significant, however, that most of our cases have neglected teeth and that the majority are heavy smokers. Syphilis is usually considered to be an etiological factor; but we have not found any greater frequency of syphilis in our group of patients than in the normal population. The food eaten is of the usual kind, not being particularly spiced and having no irritating qualities.

One gets the impression that proper dental care and elimination of smoking would probably reduce the incidence of the disease.

DIAGNOSIS AND TREATMENT

Microscopy

Usually the pathologist reports a keratinizing squamous carcinoma and only 7% of our cases have been reported

* Dr. Ralston Paterson has pointed out that owing to the lack of comparable in-patient facilities, radiotherapy cannot be given under as good conditions to non-Europeans as to Europeans. This is true and is acknowledged with regret; it probably partly accounts for the fact that we have still to meet our first successful radio therapeutic result in a non-European.

as anaplastic. In agreement with most other investigators we find that the immediate radiotherapeutic response is better in the anaplastic types though their later progress is less favourable. The keratinizing type offers better immediate prospects with surgery. On only two occasions has sarcoma of the mouth been encountered; in both instances in the upper jaw.

Diagnosis

Some of the earliest neoplastic lesions have been found in cases of *leukoplakia*. The localized heaped-up variety of this condition calls for excision and cancerous areas are discovered in about 60%. The diffuse, flatter variety of leukoplakia does not, in our experience, carry the same grave outlook and can be treated expectantly. Other early lesions are occasionally found when a tooth suddenly becomes loose or when there is unexplainable delay in the healing of a socket after an extraction.

The usual first complaint is that the patient feels as if a foreign body has penetrated the mucous membrane of the mouth. He points to a small pearly-white area; there is no pain. Very quickly the lesion ulcerates, infection takes place and pain develops. The pain is at first local, but as the lesion enlarges, the nerves supplying the tongue become involved and the pain is referred in the distribution of the trigeminal nerve, to the face and to the ear.

Difficulty in speech and in swallowing indicates that infiltration of the tongue or of the floor of the mouth has occurred, and as infection is constantly present, foetor is a pronounced feature. Occasionally blood-stained sputum or a brisk haemorrhage may draw attention to a cancerous ulcer at the back of the tongue. The protruded tongue deviates to the diseased side.

In the untreated case the tumour increases in size, the ulceration extends locally to involve adjacent portions, and very quickly the mandible is infiltrated. This infiltration takes place far quicker from a primary growth than from secondary glands.

Apart from local extension of the growth, spread by the lymphatics is very common and occurs early in the disease. The submental glands become invaded from lesions involving the floor of the mouth or the tip of the tongue, the submaxillary glands get attacked from growths of the alveoli, cheek, floor of mouth and side of the tongue and the deep cervical glands surrounding the internal jugular vein drain both submental and submaxillary glands. Owing to its anatomical proximity, the posterior part of the tongue drains almost directly into the tonsillar gland of the internal jugular chain and because of the free lymphatic anastomosis and extreme mobility of the parts, lymphatic spread occurs early and is not uncommonly bilateral.

Clinically, the glands are recognized as involved when they enlarge and become palpable. It is very difficult, however, to differentiate between an inflammatory gland and a neoplastic one and for this reason it is necessary to keep a careful watch and to take appropriate action as soon as any glandular enlargement is felt. Left alone, the glands enlarge, become adherent and ulcerate through the skin; they grow inwards and erode the carotid arteries.

Blood spread is a rare complication because in the past, few patients survived the disease long enough to

enable such a spread to be observed. However, it is now possible to report several cases in which the primary disease and its glandular metastases were kept under control for a sufficiently long time for blood-borne metastases to become apparent.

If the disease is untreated, or if treatment has not been successful, death occurs inevitably and very soon (Fig. 2) and is due to 3 main causes.

1. Inanition from inability to swallow and from the absorption of the foul discharges in the mouth.
2. Septic broncho-pneumonia from inhaled infected material.
3. Secondary haemorrhage from the primary growth eroding into the lingual artery or from the secondary glands ulcerating on to the surface and later eroding one of the carotid arteries.

Examination

As cancer of the mouth is in most cases visible and is at all times palpable, the examination of the patient should be performed in a good light. The mouth is opened as far as possible and the interior carefully inspected with mirror or torch. Careful palpation will indicate the site and size of the disease, its mobility, and whether it is attached to the mandible or not. Sometimes a woody indurated area is found with no ulceration present; this should be recognized as a possible infiltrating carcinoma. Standing behind the seated patient, it is possible to palpate the glands in the submaxillary region and the jugular chain from below the ear to the supraclavicular area, especially if one uses Lahey's manoeuvre of pushing the larynx first to one side and then to the other; the glands then become very apparent.

A piece of tissue should now be obtained for examination; any condition which arouses the slightest suspicion should be given the benefit of biopsy. It is most important to take a generous piece, which should include not only the malignant, but also a portion of the adjacent normal tissue. Several such snips should be taken, avoiding the necrotic loose area in the middle of the growth. No greater tragedy can befall a patient suffering from cancer than to have a biopsy report returned negative. If the condition appears malignant and the pathological report does not confirm the clinical impression, it is essential to take a second specimen and finally, to excise the affected area completely under a general anaesthetic. On several occasions we have had a positive report come back on the third time of asking. Since early treatment is of vital importance, it is necessary to make the pathologist aware of the position and that his reports be expedited.

Treatment

Many cases, under proper conditions and with careful and regular follow-ups can be kept under control by X-ray therapy or radium treatment. The radiotherapist aims at delivering about 6,000 Röntgen units to the tumour in a uniform dose. It has been the usual procedure where absolute indications for surgery have not been present, to give every case such a course of radiotherapy and if unsuccessful, to pass the failures on for

TABLE I. ANALYSIS OF TREATMENT GIVEN TO 120 OF THE 144 CASES. 24 (16.6%) WERE TOO ADVANCED OR REFUSED ALL THERAPY

	Radio-therapy	Radio-therapy plus surgery	Surgery
Tongue, Anterior 2/3rds	19	10	9
Tongue, Posterior 1/3rd	12	3	—
Floor of Mouth	11	6	—
Alveolus	11	7	—
Cheek	4	3	—
Tonsil	9	3	—
Palate	8	4	1

surgery. As it takes about 6 weeks for the maximum effects of radiotherapy to develop and a further few weeks before the tissues return to a sufficiently normal state to permit an operation, at least 2 months are lost before surgery can be undertaken with comfort. While radium therapy does not usually cause excessive fibrosis, a course of deep X-ray treatment as a rule adds to the technical difficulties of the operation. Although we do not usually advocate this, a strong argument could be put forward for immediate surgery in many cases, with radiotherapy to follow in those where complete eradication has not been achieved.

The operation which we perform consists of the complete removal of the primary in the mouth and of the glands in the neck in one continuous piece. This approximates very closely to the modern idea of a proper cancer operation. The glandular removal has now become reasonably standardized; in common with most surgeons we have given up suprahyoid clearances or other local removal of the glands. For these glandular excisions we follow a technique which involves clearing the anterior and the posterior triangles together with removal of the sternomastoid and the jugular vein with the associated deep cervical group.

The operations that are needed in the mouth are not standardized but must be varied to suit the individual case according to the variations in the site and extent of the primary disease. In many cases it is possible to save the jaw, but frequently a portion of the mandible, of variable size, requires removal either for access or because the bone has become directly infiltrated by the neoplasm. With this form of operation a very wide exposure is obtained, which allows us to make a radical sweep of the primary disease and prevents local recurrences. The operation is a big one but the patients tolerate the procedure very well.

As is usual in surgery of the head and neck, there is very little shock and blood transfusions can be kept down to a minimum. However, it is important that the patients, usually elderly men with cardiac disease, should be under adequate therapy to prevent decompensation. We have lost only one patient as a result of operation—a sudden death 12 hours after operation in an elderly man with cardiac decompensation.

Pneumonia has not been encountered in our series, but fistula formation was common until we insisted on nasal feeding for the first 10 post-operative days. It is our practice to do a temporary tracheotomy in all cases where the posterior part of the tongue or pharynx has been excised. This tube is removed on the 3rd or 4th

day except in those cases where the anterior part of the mandible or genio-hyoglossus has been divided, when the tracheotomy must be left in for a few days longer.

With careful management, complete healing after surgery takes place early, and 14 days after the operation X-ray treatment can be started if necessary. The wounds do not break down under this post-operative radiotherapy.

After the definitive treatment is over, the patient must be observed at regular weekly intervals for about 2 months. These intervals are gradually lengthened and at the end of a year the patients are asked to return every 6 months. On each occasion both the site of the original primary and the glands in the neck are carefully examined and instructions are given to report immediately should any lump or ulceration develop.

Prophylactic Clearance of the Glands

If it is possible to keep the patient under careful and frequent observation, we do not consider that routine prophylactic clearance of the glands is justified. Many of our cases however come from the more remote parts of the country and not a few lack sufficient intelligence to return for regular follow-ups; in these cases we do not hesitate to advise a prophylactic clearance on the same side as the disease.

Palliation

Where it is obvious that a radical cure will not be achieved by operation, a palliative procedure will still afford the patient relief. A hemiglossectomy will often allow the primary condition to be kept under control even though the secondary glands prove to be irremovable. As the lingual and the inferior alveolar nerves are usually excised with the primary tumour, there is often considerable relief of pain after the operation. Palliative radiotherapy is then given to the glands as well as to the operated area after healing has taken place. In those patients where local recurrence has occurred after surgery, more radiotherapy may be safely given in normal doses because, the previously irradiated area having been removed, the site of local recurrence is, from the radiotherapeutic point of view, virgin soil.

Where this second course of radiotherapy fails and pain is a prominent feature, we have referred the patients to the neuro-surgeons for glosso-pharyngeal and Gasserian neurectomies, Gasserian injections and, in some cases, pre-frontal lobotomy.

We have not found local cauterization by any method, or incomplete local excision with the diathermy, to be of any lasting value in the relief of pain.

Results

An analysis is presented of 144 cases of carcinoma of the mouth treated over the last 6 years. The analysis by race and sex is shown in Table II. Ten per cent of our patients are over 80 and a further 27% are over 70 (Fig 1), so that 5-year cures in the accepted sense is, in these patients at any rate, often of academic importance only. The elderly patient will accept a certain amount of deformity with equanimity as long as he can be promised freedom from pain and a reasonable chance of local non-recurrence. We have found that division and removal of portions of the mandible has not interfered with the

TABLE II. ANALYSIS OF 144 CASES BY RACE AND SEX

	E.M.	E.F.	C.M.	C.F.	N.
Tongue, Anterior 2/3rds	20	5	16	3	1
Tongue, Posterior 1/3rd	9	0	4	0	2
Floor of Mouth	14	2	5	0	2
Alveolus	6	0	6	9	3
Cheek	4	0	2	2	0
Tonsil	7	0	6	1	0
Palate	6	2	4	0	3

E=European. C=Coloured. N=Native. M=Male. F=Female.

normal diet of our patients, and these operations, from the functional point of view, permit the patients to lead a normal and comfortable life. Speech and swallowing return very soon and the patients pick up condition remarkably quickly.

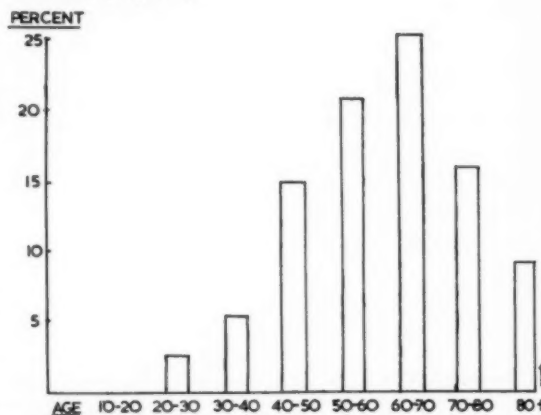


Fig. 1. Age incidence of 144 cases of C.A. of the mouth.

We have excised portions of the mandible for malignant disease on 37 occasions and done a complete gland clearance (Bloodgood) in 26 cases. Our mortality has been the one case mentioned above. We have carried out 27 cases of suprahyoid and submaxillary clearance before we went on to the more radical operation, and 21 glossectomies; all without mortality.

In contrast to the average survival time of untreated cases and of those who have failed to respond to therapy, we are able to present not a few individual results which are relatively satisfactory by comparison (Fig. 2). These

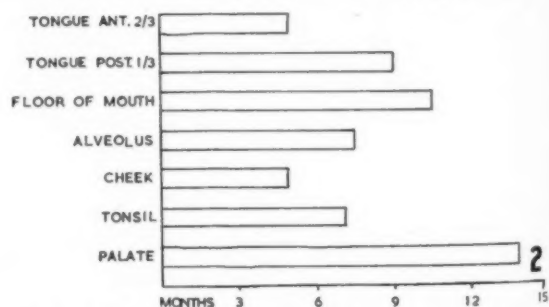


Fig. 2. Average survival in months of untreated cases and of cases that have failed to respond to therapy.

figures are not statistically significant because the work has not been in progress long enough to allow us to establish 5-year survivals, but the results have shown that with careful team-work and cooperation between radio-therapist and surgeon, a considerable amelioration of symptoms can be achieved in most patients and that many can be completely cured. The results of treatment according to the site of the primary carcinoma are shown in Fig. 3.

mutilations can then to a great extent be avoided and the ultimate results very much improved.

SUMMARY

1. The management of carcinoma of the mouth is discussed.
2. A plea is made for earlier diagnosis and for more radical surgical methods in certain types of cases.

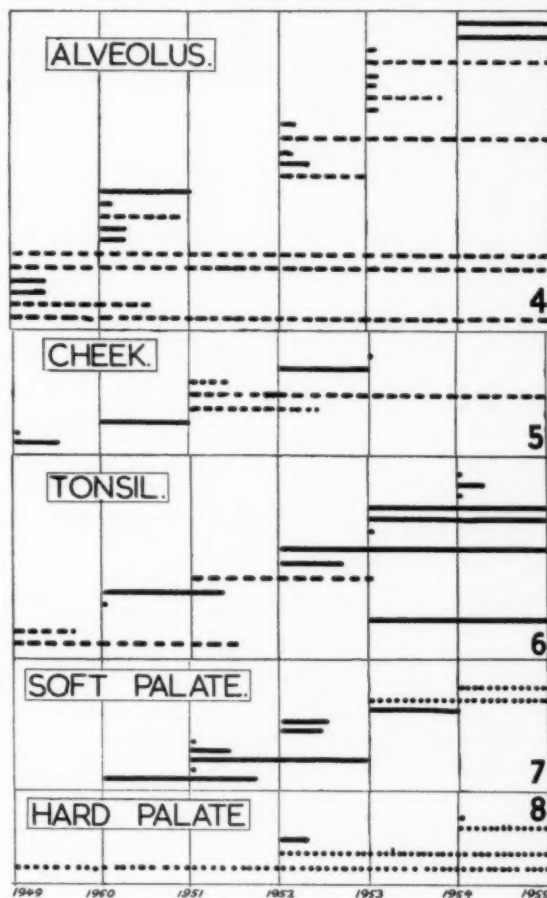
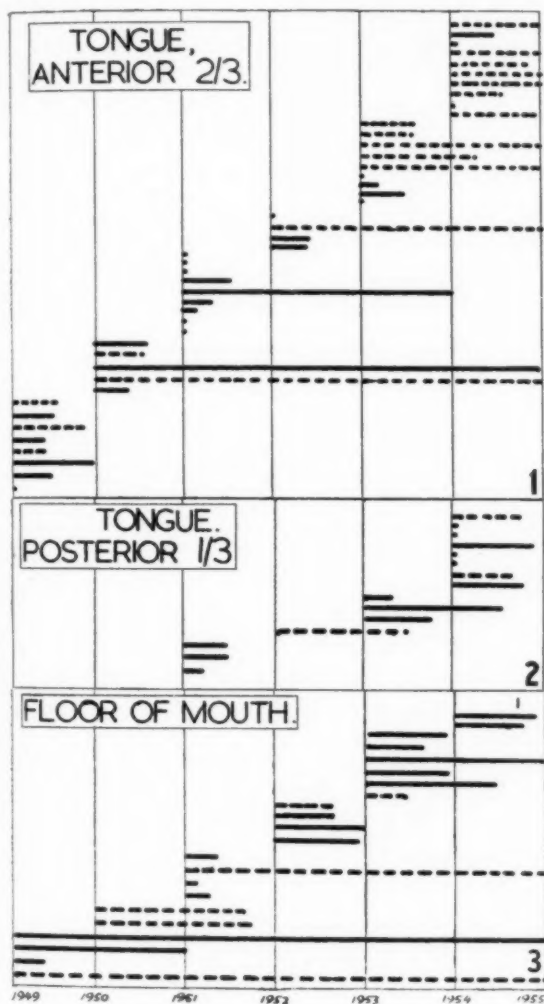


Fig. 3. Results of treatment. Continuous lines—radiotherapy. Broken lines—surgery performed.

It must be emphasized that in contrast to the cases appearing at overseas clinics, at least 50% of our cases present themselves for the first time with fixed glands or with adjacent parts deeply invaded with neoplasm; for such cases nothing can be offered apart from sedatives. One cannot help feeling that, with more intensive propaganda and improved education, more patients will present themselves in the earlier curable states. The extensive

3. An analysis of 144 cases treated over the last 6 years is presented.

4. The results show that with carefully selected cases and with proper team-work, much can be offered to individual patients.

I should like to thank Dr. J. M. Grieve, Head of the Department of Radiology and Radiotherapeutics at Groot Schuur Hospital, Cape Town, for his kindly interest in this work and the radio-therapists Dr. R. D. Tucker and Dr. M. B. Bennett for their enthusiastic assistance and cooperation.

UNIVERSITY OF THE WITWATERSRAND MEDICAL GRADUATE ASSOCIATION

A course of instruction in clinical psychology for medical practitioners has been arranged by the Medical Graduates' Association in conjunction with the General Practitioners' Group of the Medical Association of South Africa. The course will last from the end of February until early December 1956, with a vacation in July.

The fee is expected to be approximately £10 10s. 0d. payable in advance. Practitioners desiring to attend should communicate with the Honorary Secretary of the Medical Graduates' Association, Medical School, Hospital Hill, Johannesburg, from whom a detailed syllabus may be obtained (telephone 44-7040, mornings only).

Lectures will be given on two evenings a month at an easily accessible venue, from 8 p.m. to 10.15 p.m. The lecture period is

to be divided into two sections: (1) A didactic lecture for one hour and (2) a group discussion and seminar devoted to patients and problems arising in the daily life of the practitioner. It is also intended to devote certain evenings to demonstrations of actual cases, and later in the course specialists in psychiatry and psychology are to contribute.

The course is intended primarily to acquaint the general practitioner with the patient as a living dynamic entity within the framework of his own environment.

Reference will be made to the psychology underlying clinical entities such as cardiac neuroses, neuroses in gynaecology and obstetrics, sexual maladjustments, childhood complaints such as enuresis, feeding difficulties, etc., asthma, and the typical psychoneuroses.

PASSING EVENTS : IN DIE VERBYGAAN

Mr. S. R. Taitz, F.R.C.S., is now in practice as a thoracic surgeon at 320 Eagle Star House, Salisbury Arcade, West Street, Durban. Telephone, rooms 63297, after hours 29326, residence 36402.

* * *

Dr. Lewis S. Robertson has been elected Chairman of the Johannesburg Hospital Board to succeed Mr. Hugh R. Solomon who resigned for health reasons after 25 years service as its chairman.

* * *

Messrs. Parke, Davis and Company are planning to build a new medical research centre at Detroit, Mich., at a cost of about 10 million dollars. It is estimated that planning and construction will extend over 3 years. Much important medical research has been carried out in the laboratories of the great drug houses. Amongst the drugs that Messrs. Parke Davis have discovered or elaborated are Taka-Diastase (1895), Pituitrin (1909), Theelin (1930), Mapharsen (1934), Epanutin (1938), Promin (1945), Chloromycetin (1948), Camoquin (1952) and Milontin (1953).

* * *

The Southern Africa Cardiac Society was formed at an inaugural meeting on 2 February 1956. The Committee of the Cape Province Section was elected as follows: *Chairman*—Dr. Maurice Nellen. *Secretary*—Dr. Louis Vogelpeel. *Treasurer*—Dr. Val Schrire. *Executive Members*—Professor Frank Forman and Dr. David Le Roux.

* * *

Mr. T. Holmes Sellors, D.M., M.Ch., F.R.C.S., Thoracic Surgeon, Middlesex Hospital, London, will be visiting Johannesburg from 18 February to about 28 February, and has agreed to deliver a lecture under the auspices of the American College of Chest Physicians (Northern Chapter of South Africa) on Wednesday, 22 February at 8.15 p.m. in the Harveian Lecture Theatre at the Medical School. He will talk on one of two subjects: *The Recent*

Advances in Thoracic Surgery, or Intra-Cardiac Surgery. A welcome is extended to all medical practitioners and specialists who wish to attend.

* * *

Royal Society of Tropical Medicine and Hygiene. In 1957 it will be 50 years since the foundation of this Society by Sir Patrick Manson, Sir James Cantlie, Sir Ronald Ross, Sir David Bruce and other eminent men in the field of tropical medicine. The Society is at present desirous of extending its membership. The annual subscription for fellows is £2 10s. 0d. per annum, which includes the Transactions, 6 numbers of which make up the yearly volume of some 800 pages. This journal has become the medium for much valuable work in tropical medicine and allied subjects. Other privileges of fellows include admission to the Society's meetings at its house (Manson House) at 26 Portland Place, London, W. 1, where rooms are set apart for reading, writing and other purposes. Election to fellowship in the Society is made by the Council on the recommendation of two fellows. The local representatives in South Africa are Dr. R. Elsdon-Dew in Durban, Dr. J. H. S. Gear in Johannesburg and Prof. J. F. Brock in Cape Town.

* * *

Dr. Michael Denny, M.B., B.Ch. (Cape), D.M.R. (Lond.), who has for the past 8 years been radiologist to the Addington and King Edward VIII Hospitals, Durban, and the Baragwanath and General Hospitals, Johannesburg, has joined Drs. Samuel, Komins and Morris in radiological practice at 1 Lister Buildings, Jeppe Street, Johannesburg.

Dr. Michael Denny, wat vir die afgelope agt jaar as Radioloog vir die Addington en King Edward VIII hospitale te Durban, as ook die Baragwanath en Algemene hospitale te Johannesburg opgetree het, het by Drs. Samuel, Komins en Morris in radiologiese praktyk aangesluit. Adres: 1 Lister Gebou, Jeppe Street, Johannesburg.

BOOK REVIEWS : BOEKRESENSIES

THE ACUTE PHASE OF POLIOMYELITIS

Diagnosis and Treatment of the Acute Phase of Poliomyelitis and its Complications. Edited by Albert G. Bower, M.D. Pp. 250 with 64 illustrations. 50s. London: Baillière, Tindall and Cox. 1954.

Contents: 1. A Modern Concept of the Treatment of Acute Poliomyelitis with Particular Reference to Cases with Respiratory Insufficiency. 2. Diagnosis and Differential Diagnosis of Poliomyelitis. 3. Medical Management of the Patient with Acute Poliomyelitis. General Considerations. 4. The Role of the Otolaryngologist in the Treatment of Poliomyelitis. 5. Pulmonary Complications of Acute Poliomyelitis with Respiratory Insufficiency from an X-ray Standpoint. 6. Observations on Prevention and Treatment of Pulmonary Complications of the Tracheotomized Respirator Patient. 7. The Detection and Care of the Patient

with Respiratory Difficulty. 8. Special Nursing Procedures for Respiratory Poliomyelitis Patients. 9. Physical Medicine in the Treatment of Acute Poliomyelitis. 10. The Role of the Obstetrician in the Treatment of Poliomyelitis. 11. Mechanical Apparatus. 12. Transfer of Respirator Patients to Other Locations. 13. Biochemistry and Electrolyte Changes in Poliomyelitis. 14. Orthopedic Treatment, Including Bracing. 15. Experiment and Experience of the Poliomyelitis Team of the Washoe County Medical Society, Reno, Nevada. Index.

This book, edited by Dr. Albert G. Bower, is written by 14 expert contributors, 11 of whom are members of a team attached to the Los Angeles County Hospital—the second largest hospital for communicable diseases in the USA. The clinical management and technique employed in the treatment of patients in the acute phase of poliomyelitis is described in detail and based on experience gained by the members of this team from the treatment of 17,000

cases at this hospital (11,000 have been treated during the past 7 years).

Whilst all the main clinical aspects are very adequately dealt with, it is felt that the chapters on the Medical Management of the Acute Poliomyelitis Patient, the Detection and Care of the Patient with Respiratory Difficulty, and the Biochemistry and Electrolyte Changes in Poliomyelitis, are particularly useful. Throughout the book the need for early tracheotomy in bulbar cases with respiratory embarrassment is emphasized if the mortality in 'wet' bulbar poliomyelitis is to be reduced. The book also includes valuable contributions by the otolaryngologist, radiologist, physical medicine expert, orthopaedic surgeon, and obstetrician. Various types of mechanical apparatus used on the patient requiring artificial respiration are described and their value assessed.

The book is well and concisely written and contains many excellent instructive illustrations. It is felt that it will be of general interest to all doctors, and particularly useful and informative to those who are called upon to treat patients with acute poliomyelitis in hospital.

D.M.K.

MEDICAL STATISTICS

Principles of Medical Statistics. Sixth edition. By A. Bradford Hill, C.B.E., D.Sc., Ph.D., F.R.S. Pp. 314 + ix. 10s. 6d. London: The Lancet Ltd. 1955.

Contents: 1. The Aim of the Statistical Method. 2. Selection. 3. Presentation of Statistics. 4. The Average. 5. The Variability of Observations. 6. Calculation of the Standard Deviation. 7. Problems of Sampling: Averages. 8. Further Problems of Sampling: Proportions. 9. Further Problems of Sampling: Differences. 10. Further Problems of Sampling: χ^2 . 11. Further Examples and Discussions of χ^2 . 12. The Coefficient of Correlation. 13. Calculation of the Correlation Coefficient. 14. Life Tables and Survival after Treatment. 15. Common Fallacies and Difficulties. 16. Further Fallacies and Difficulties. 17. Calculation of Standardized Death-Rates. 18. Calculation of Standardized Indices. 19. Clinical Trials. 20. General Summary and Conclusions. Index.

In the 1st edition of this admirable book on medical statistics, the author discussed the problem of clinical trials in his chapter 'General Summary and Conclusions'. In this 6th edition, which appears 18 years later, he has devoted a new chapter to this subject, in which the topic is discussed in detail. It is of very great importance today since every doctor's post-box overflows with advertisements from drug houses claiming greater efficacy for their products.

Medical practitioners have a rather ostrich-like attitude to statistics, often because they don't understand the subject and are frightened by the magical mathematical symbols they see written in articles.

The brilliance of this book is that it can be read by the non-mathematically minded individual (such as the reviewer) and yet be enjoyed and understood. The writing is crystal clear and simple and the illustrations well chosen to interest a large reading public.

Most of the book is devoted to the techniques which the statistician employs in presenting and in interpreting figures. A great deal of discussion revolves round the meaning of 'significance' of difference between two sets of figures, and to the inferences that can be drawn from such differences.

Dr. Bradford Hill emphasizes time and again the care which investigators must take to ensure that the data they compare are in fact comparable. He also emphasizes the application of common sense and logic to the interpretations of the figures.

This slim volume is packed with wisdom presented in an eminently readable form and should be owned by every undergraduate and postgraduate student of medicine.

E.J.S.

BONE AND BONES

Bone and Bones. Fundamentals of Bone Biology. Second edition. By Joseph P. Weinmann, M.D. and Harry Sicher, M.D., D.Sc. Pp. 508 with 302 illustrations. South African price £5 17s. St. Louis: The C. V. Mosby Company. 1955.

Contents: Part I. Normal Structure and Growth of Bone and Bones. 1. Bone Tissue. 2. Bones. Part II. Pathology of Bone and Bones. 3. Developmental Disturbances of the Skeleton. 4. Adaptational Deformities of the Skeleton. 5. The Influence of Endocrine Glands on Bone and Bones. 6. The Influence of Vitamins on Bone and Bones. 7. The Effect of Minerals on Bone and Bones. 8. Healing of Bones. 9. Necrosis of Bone and Inflammation of Bones. 10. Tumors of the Skeleton. 11. Idiopathic Lesions of the Skeleton. References.

This book with the odd title, ('bone is a tissue; bones are organs') is particularly memorable for large numbers of magnificent photomicrographs. Although none of them are in colour their detail and definition is such that the various structures, fibrils, cells and

so on stand out from each other in superb clarity. This applies to every photograph—there is not a single mediocre one.

In comparison the text is rather pedestrian. It is, where the reviewer is able to judge, good and accurate; in places, rather hard to follow. It certainly is not a book to read straight through. There does not seem to be anything new or particularly remarkable in it. There is disappointingly little on hyperthyroidism or on osteoporosis, but it is a pleasure to see terms correctly used. The conception of osteogenesis imperfecta as 'congenital osteoporosis' is a good one, and in accord with modern views.

The section on acromegaly is most outstanding. The mechanisms of the various deformities found in this condition are explained in detail.

There are few X-ray reproductions in this book—it is written by a pathologist and an anatomist in collaboration. It can, nevertheless, be heartily recommended to the radiologist; also to the pathologist, the orthopaedic surgeon and the physician interested in bone or bones.

P.J.

MEDICAL GENETICS

Counseling in Medical Genetics. By Sheldon C. Reed. Pp. 268 + viii. \$4.00. Philadelphia & London: W. B. Saunders Company. 1955.

Contents: 1. 'In the Beginning'. 2. What are the Problems? 3. A Philosophy for Counseling. 4. A Few Laws. 5. Twins. 6. Don't Marry a Relative! 7. The Ubiquitous Heterozygote (or, The Common Carrier). 8. Mongolism. 9. Nervous System Malformations. 10. Clubfoot. 11. Harelip and Cleft Palate (of Mice and Men). 12. Congenital Heart Disease. 13. Mental Retardation. 14. String Beans and Chubbies. 15. Pyloric Stenosis. 16. Congenital Dislocation of the Hip. 17. Fibrocystic Disease of the Pancreas. 18. Blood Genetics. 19. Disputed Paternity. 20. Skin Color. 21. Convulsive Seizures. 22. Rheumatic Fever. 23. Tuberculosis. 24. Allergies. 25. Diabetes. 26. Schizophrenia. 27. Manic-Depressive Psychosis. 28. Genetic Effects of Radiations. 29. Putting the Puzzle Together. Appendix. Index.

Here at last is a really easy book on medical genetics. No one, absolutely no one, not even you, need be scared of it. It is to be feared that there is a considerable amount of ignorance even among our own ranks on this subject, together with misconceptions and misuse of terms like 'familial' and 'hereditary'. This book takes us from the beginning in a practical way, always with the main theme in mind. The main theme is the advice (or 'counseling') which we, as doctors, should give when consulted on a genetic problem.

I thoroughly recommend that it should be read by all of us. It could with profit be read by intelligent laymen. It appears to be highly accurate and up to date. The reviewer has found two things to quibble about; one on p. 103, the rather slighting reference to breast feeding and one on page 197, the too easy acceptance of foetal loss in a diabetic mother.

Works on medical genetics are usually written either by a doctor who knows little genetics or by a geneticist who knows even less medicine. The author here appears to understand both disciplines.

W.P.U.J.

PRIMARY ANATOMY

Primary Anatomy. Third Edition. By H. A. Cates, M.B. and J. V. Basmajian, M.D. Pp. 339 + xii, with illustrations and plates. 46s. 6d. London: Baillière, Tindall and Cox Ltd. 1955.

Contents: 1. Introduction. 2. Skeletal System. 3. Articular System. 4. Muscular System. 5. Digestive System. 6. Respiratory System. 7. Urinary System. 8. Generative or Reproductive System. 9. Circulatory System. 10. Nervous System. 11. The Eye. 12. The Ear. 13. Skin and Endocrine Glands.

A knowledge of Anatomy is required by many students other than those studying medicine, and this text-book supplies their need. It is intended for nurses, occupational therapists, physiotherapists and all those requiring an elementary knowledge of human anatomy. There are but few text-books which fill the need for these students. Nurses sometimes have to rely on books intended for school children or written for First-Aid or Home Nursing classes, which are obviously too superficial and simple. This book supplies all the necessary information needed by these non-medical students and is sufficiently comprehensive to satisfy the most seeking amongst them.

The choice of a systematic rather than a regional approach is greatly to be recommended. This produces clarity and continuity and introduces a good deal of physiology at the same time.

The book is generously illustrated and the drawings are of the bold, clear and schematic type where every picture tells a story.

P.J.M.R.

BOOKS RECEIVED : BOEKE ONTVANG

The Aetiology of Epidemic Infantile Gastro-Enteritis. By J. Smith, M.D., D.Sc., F.R.C.P. (Lond.), D.P.H. Pp. 104, with illustrations. Edinburgh: The Royal College of Physicians. 1955.

Year Book of Pediatrics. (1955-1956 Year Book Series.) By Sydney S. Gellis, M.D. Pp. 431, with illustrations. Chicago: The Year Book Publishers. 1955-1956.

The Compend. Compiled by W. Hetherington, F.P.S. Pp. 669. Bristol: John Wright & Sons Ltd. 1955.

Elementary Physics. By G. Stead, M.A. (Cantab), D.Sc. (Lond.), F.Inst.P. Ninth Edition. Pp. 532, with 448 illustrations. London: J. & A. Churchill Ltd. 1955.

Refresher Course for Practitioners. Specially Contributed Articles from the Journal of the Indian Medical Association. Volume I. Pp. 364, with illustrations. 8s. Calcutta: Tarani Kanta Basu. 1955.

Modern Public Health for Medical Students. By I. G. Davies, M.D., F.R.C.P., D.P.H. Pp. 487, with illustrations. 30s. London: Edward Arnold (Publishers) Ltd. 1955.

The Midwife's Text-Book. Seventh Edition. By R. W. Johnstone and W. I. C. Morris. Pp. viii + 396, with 219, illustrations. London: A. & C. Black. 21s. net. 1955.

A Text-Book of Midwifery. Sixteenth Edition. By R. W. Johnstone and R. J. Kellar. Pp. xvi + 582, with 295 illustrations. 25s. net (S.A. Price 36s.). London: A. & C. Black. 1955.

Rehabilitation of a Child's Eyes. By Richard G. Schober, B.A., M.D., F.A.C.S. Pp. 133, with illustrations. \$2.85. St. Louis: The C. V. Mosby Company. 1955.

The Laboratory Diagnosis of Cancer of the Cervix. Edited by F. Homburger, M.D. and W. H. Fishman, Ph.D. Basle (Switzerland), New York: S. Karger. 1956.

A Hundred Years of Nursing. By Sir Zachary Cope. Pp. 144, with illustrations. 10s. 6d. London: William Heinemann Medical Books Ltd. 1955.

Donne e fanciulli meno felici. By I. e G. Calderoli. Pp. 231, with illustrations. Bergamo: Scuole Professionali T.O.M.

Bulletin of the World Health Organization. Pp. 742, with illustrations. 10s. Geneva: The World Health Organization. 1955.

CORRESPONDENCE : BRIEWERUBRIEK

CAPE SCHOOL FOR CEREBRAL PALSID CHILDREN

To the Editor: In my letter¹ which you so kindly published in the *Journal* of 28 January, the school was not given its correct title, and was merely referred to as a centre for cerebral palsied children. I wonder if you would mind clarifying this point so that readers will have no doubt about the school's title.

Cape School of Cerebral Palsied Children

'Keerweer'
Meadow Road,
Rosebank, Cape
6 February 1956

C. W. Coplans
Chairman
Medical Advisory Committee

1. Coplans, C. W. (1956): *S. Afr. Med. J.*, **30**, 94

CORONARY THROMBOSIS AND DIETARY FAT

To the Editor: Before some of our over-enthusiastic colleagues suggest castration as a means of avoiding an early demise from arterial degeneration (Russ, E. M., Eder, H. A. and Barr, D.P. (1955): *Amer. J. Med.*, **19**, 4), may I utilize the columns of the *Journal* to raise a protesting voice against the major line in present-day research on the subject.

Any general research which uses, as a fundamental, a variable such as dietary fat, which is subject not only to racial, but to individual idiosyncrasy, as well as familial, social and possibly physiological variations, is in the final analysis going to prove but one thing—some people die of coronary disease and some don't.

Surely the only one pertinent, apparent and statistically unassailable inference that can at present be drawn, is that *the darker the skin, the less the liability to arterial degeneration*. I, personally, can face the possibility of death from a coronary thrombosis with more equanimity by attributing it to the vagaries of Nature, than the silent assumption of my colleagues that it is due to an uncontrolled predilection for 'fats', a word which, these days, carries with it the stigma of gluttony.

Rooiberg Minerals Development Co. Ltd.
P.O. Rooiberg
Via Warmbaths, Transvaal

E. Baskind
Medical Officer

MITRAL VALVOTOMY

To the Editor: Dr. Schrire and his associates¹ were apparently reluctant to reply to our letter² because they believed that the facts as published spoke for themselves. Having read their reply, we feel that not only did the original facts not speak for themselves, but many of the statements made in the reply are incorrect and misleading and add to confusion already created.

Dr. Schrire *et al.* have not quoted us correctly; we stated that 6 of our patients were in congestive failure *at the time of operation*. Many more of our cases were in grade 4 (defined by Wood³ as totally incapacitated patients), and even though they may have had chronic congestive failure, in the great majority the failure could be relieved by pre-operative intensive medical treatment. Similar experiences were mentioned by Sellors *et al.*⁴ in their series of 150 patients, and they listed, amongst their contraindications to operation, congestive heart failure which could not be relieved by medical treatment. We remain surprised that 17% of the patients in the series of Dr. Schrire *et al.* were in congestive heart failure *at the time of operation*. We would further point out that while Dr. Schrire *et al.* report an immediate mortality of 4 cases (31%, not 28% as published) and a total mortality of 7 cases (54%, not 49% as published) in their grade-4 patients, they do not mention the results in the survivors in this group, and thus their statement that '... if one is interested in keeping the mortality figure down, only the best-risk cases are chosen and many patients who might benefit are refused surgery' is totally uncalled-for and unjustified by fact.

We are again misquoted as believing that 'a high pulmonary artery pressure simply means a high pulmonary arteriolar resistance...'. The presence of a raised pulmonary arteriolar resistance in 61.6% of surgical cases and 40% of all cases of mitral valve disease in Wood's series⁵ confirms that considerably more than a small proportion of cases develop a 'second obstruction'. It is worthy of note that in the above series, all patients with a pulmonary arterial systolic pressure above 100mm. Hg had marked increase of the pulmonary arteriolar resistance.

Even if Dr. Schrire *et al.* are not satisfied with an excellent result in 2 and a good result in 1 out of 5 patients with slight incompetence pre-operatively, their free admission that the figures may not be statistically significant substantiates our objection to the statement, as originally published, that 'the presence of incompetence, even if slight considerably reduces the chances of success' (italics ours).

701 Ingram's Corner
Kotze and Twist Streets
Johannesburg
3 February 1956

M. M. Zion
B. A. Bradlow

1. Schrire, V., Vogelpoel, L., Phillips, W. and Nellen, M. (1956): *S. Afr. Med. J.*, **30**, 94 (28 January).
2. Zion, M. M. and Bradlow, B. A. (1955): *Ibid.*, **29**, 1244 (24 December).
3. Wood, P. (1954): *Brit. Med. J.*, **1**, 1051.
4. Sellors, T. H., Bedford, D. E. and Somerville, W. (1953): *Ibid.*, **1**, 1059.
5. Wood, P. (1954): *Ibid.*, **1**, 1113.